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Sugar Deoxygenation

Assessing the Optimal Deoxygenation Pattern of Dodecyl Glycosides for Antimicrobial Activity Against *Bacillus anthracis*

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Dedicated to the memory of Professor Dr. Derek Horton in recognition of his outstanding contributions in the subject of industrial carbohydrate chemistry.

Abstract: The discovery of the bactericide dodecyl 2,6-dideoxypyranoside reorganizing membrane phospholipid matrix of *Bacillus* species into a hexagonal phase, encouraged further research on glycone deoxygenation/bioactivity relationship. We now describe expedient syntheses of new 2-, 3-, 4-deoxy, 2,3- and 3,4-dideoxy glycosides in moderate to good yields. Interestingly, Amberlyst 15 is a key protagonist, efficiently applied for the transacetalation of alkyl deoxy glycosides and for ring contraction to access regioselectively hexofuranosides. The 2-deoxy-D-*arabino* pyranoside affords the higher MIC values against two *Bacillus* spp. and *Enterococcus faecalis*, while a 4-fold decrease or higher was found by inversion of configuration or by deoxygenation at C-3. While 2,3- and 3,4-dideoxygenation do not improve bioactivity, the 4,6-dideoxy-α-D-*xylo*-hexopyranoside remains a promising glycoside, presenting low MIC values for all species tested, and low cytotoxicity in intestinal and liver cell models.

Introduction

One of the main societal challenges of the present century is the unstoppable rise of antimicrobial resistant bacteria. *Bacillus* genus comprises a variety of pathogenic species, namely *B. anthracis* and *B. cereus*, which despite the genetic similarity, rise diverse concerns. The first causes the infectious disease anthrax affecting animals and humans, and is a serious bioterrorism threat.[1] The latter is responsible for food poisoning and generates biofilms, particularly important in implanted medical devices, triggering chronic wounds, persistent infections and creating a physical barrier to antibiotics.[2] The apprehension with the emergence of antibiotic-resistant bacterial strains led to a renovated interest in the search for antibiotics exhibiting structures prone to different mechanisms of action.

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In this context, research in carbohydrate-based antibiotics provides structural diversity and unique physicochemical properties. In the last decade, our research group has introduced a new family of alkyl deoxy glycosides, some of which exhibiting a potent activity against *Bacillus* spp. Both dodecyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside (**1**) and 2,6-dideoxy-α-D-*arabino*-hexopyranoside (**2**) are active against *Bacillus* spp., in particular *B. cereus* and *B. anthracis* (MIC 12.6 μM for **1**, and 50 μM for **2**) (Figure 1) .[3,4] Surprisingly, the 6-hydroxylated analogue **3** was not active on *B. cereus*, although it exhibited surface activity parameters such as critical micelle concentration, adsorption and aggregation data of the same order of magnitude as those of compound **2**,[3] suggesting that there is no causal link between surface activity and the mode of action. Indeed, the unprecedented mode of action underlying membrane disruption, that results from membrane permeabilization by local induction of phosphatidylethanolamine reorganization from lamellar to inverted hexagonal phases may explain this behaviour.[4]

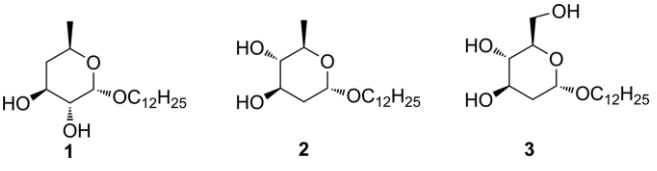


Figure 1. Alkyl deoxy glycosides active on *Bacillus* spp: dodecyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside (**1**), dodecyl 2,6-dideoxy-α-D-*arabino*-hexopyranoside (**2**) and dodecyl 2-deoxy-α-D-*arabino*-hexopyranoside (**3**).

Thus, aiming at recognizing the optimal deoxygenation pattern for antimicrobial activity, this paper describes a series of

analogues to compounds **1–3** to fully explore the potential of deoxy glycosides as new antimicrobials.

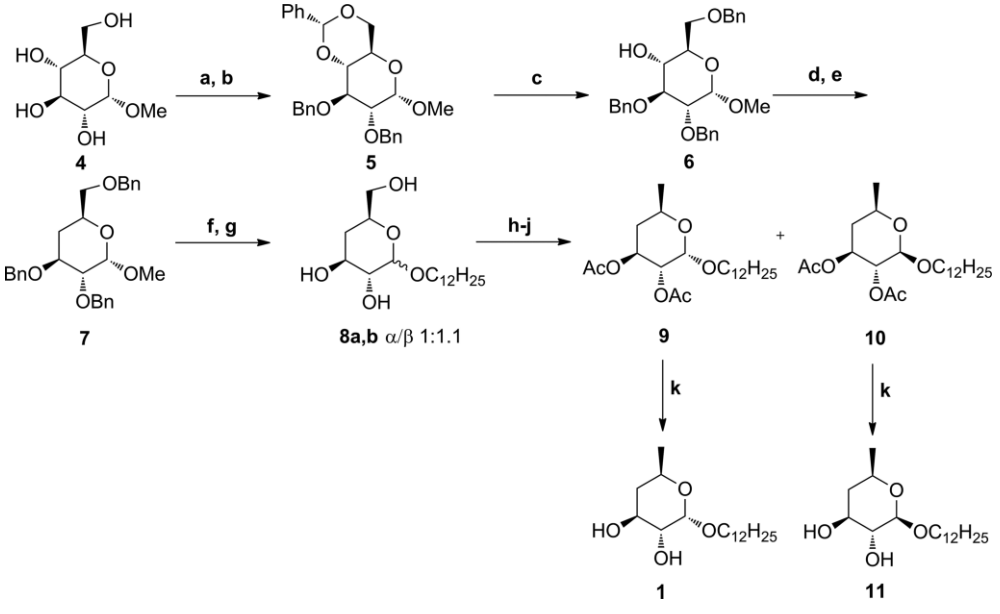
Synthetic methodologies towards dodecyl 2-, 3-, 4-deoxy, and 2,3-, 3,4-, and 4,6-dideoxy glycosides were investigated. Glycoside antimicrobial activity against *Bacillus* species and *Enterococcus faecalis* was assayed and the most promising structures confronted with in vitro cytotoxicity in intestinal and liver cell models.

Results and Discussion

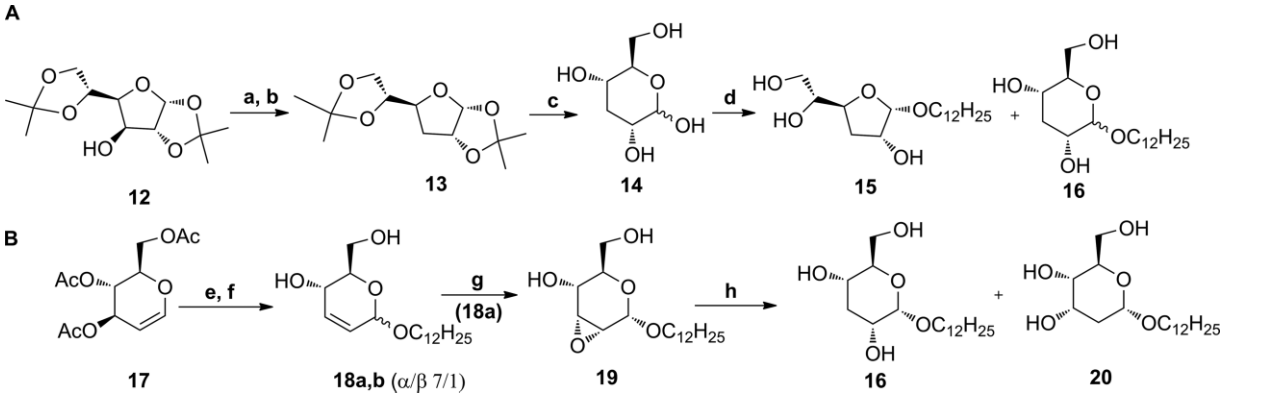
Chemistry. Synthesis of 4-deoxy glycosides starts by the transformation of methyl α-D-glucopyranoside to access position 4 free for further manipulation. Conventional benzylidenation, followed by benzylation of the free positions and selective benzylidene ring opening affords the substrate which is converted into a triflate and reduced with tetrabutylammonium borohydride (Scheme 1). The resulting 4-deoxy glycoside precursor **7** reacts with dodecan-1-ol, in the presence of Amberlyst 15. This effective and clean methodology, described by Corma and co-workers for the conversion of cellulose into biodegradable surfactants,[5] is herein adapted as an efficient glycochemistry tool, by avoiding multistep syntheses for the insertion of good leaving groups in glycosylation donor. Benzyl deprotection gives the anomeric mixture **8a**,**b** in good yield. 6-Deoxygenation succeeded with triflation and reduction, since selective tosylation failed to meet the expectations. The resulting anomers could only be separated after acetylation to give **9** and **10**, isolated by CC. Deacetylation afforded the target 4,6-dideoxy glycosides **1** and **11** in high yield.

Deoxygenation of position 3 is also investigated (Scheme 2). In the first approach, the 3-deoxy sugar **14** is prepared via triflation and reduction of diacetoneglucose (DAG) followed by isopropylidene hydrolysis (Scheme 2A). It is then used directly as a glycosyl donor in Fisher glycosylation of dodecan-1-ol. As acid promoters, Amberlyst 15, IR-120, Dowex-50R, and the clay montmorillonite were tested. With this approach pyranoside **16** is the minor product, isolated only up to 10 %. Interestingly, the major reaction product embodies a furanose ring, and the highest yield is obtained with Amberlyst 15 as promoter, revealing its versatility for this glycosylation reaction. These results are in line with those obtained by our group with other heterogeneous catalysts, namely with acid zeolites as promoters of hexopyranose acetalation.[6] Despite the low yield (28 %), this method afforded a direct access to the thermodynamically less stable furanoside as a major reaction product, thus allowing to have insights into the five-membered vs. six-membered ring impact on bioactivity/selectivity. This reaction outcome prompted us to develop a second approach to access **16**, starting with the conversion of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**17**) in the 2,3-unsaturated dodecyl glycosides **18a,b** (Scheme 2B). The α-anomer **18a** was selectively oxidized with *m*-CPBA into epoxide **19**, which reduction with $LiAlH_4$ gave the 3- and 2-deoxy glycosides **16** and **20**, in 20 % and 33 % yield, respectively. The configuration of the epoxide **19** was first proposed due to a strong correlation of H-3 with H-4 observed in the NOESY spectrum, together with the coupling constants $J_{3,4}$ and $J_{2,3}$. NMR spectroscopic data of the resulting reduction products allowed structural assignment of 2-and 3-deoxygenation, in particular the axial H-3 NMR signal of **16**, exhibiting $J_{3ax,4ax}=J_{2ax,3ax}=J_{3ax,3eq}$ = 11 Hz.

Synthesis of the dideoxy glycoside **23** (Scheme 3) was accomplished by hydrogenation of the benzyl protected Ferrier product **22a**, which was prepared by reacting a benzyl protected glycal with dodecan-1-ol in the presence of zeolite HY. The elimination of benzyl alcohol is not common when Lewis acids are used. However this heterogeneous catalyst is able to

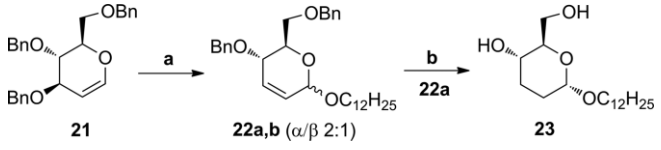


Scheme 1. Synthesis of dodecyl 4-deoxy and 4,6-dideoxy-D-*xylo*-hexopyranosides. a) $PhCH(OMe)_2$, *p*-TsOH, DMF, 60 °C, 240 mbar, 94 %; b) BnBr, NaH, DMF, 82 %; c) $NaBH_3CN$, I_2, MeCN, 77 %; d) Tf_2O, py, DCM, –10 °C; e) nBu_4NBH_4, THF, 83 % (over two steps); f) $C_{12}H_{25}OH$, Amberlyst 15; g) Et_3SiH, 10 % Pd/C, EtOAc, 80 % (over two-steps); h) Tf_2O, py, DCM, –10 °C; i) $LiAlH_4$, THF; j) Ac_2O, py, DMAP; (41 % over 3 steps); k) NaOMe, MeOH (94–96 %).



Scheme 2. **A.** Synthesis of dodecyl 3-deoxy-α-D-*ribo*-hexopyranoside and -hexofuranoside, via Fisher glycosylation. a) Tf_2O, py, DCM, –10 °C; b) nBu_4NBH_4, THF, 72 % (over two steps); c) 80 % TFA, 90 %; d) $C_{12}H_{25}OH$, Amberlyst 15, reflux (**15**, 28 %; **16**, 8 %). **B.** Synthesis of dodecyl 3-deoxy-α-D-*ribo*-hexopyranoside via epoxide. e) $C_{12}H_{25}OH$, $BF_3{\cdot}Et_2O$; f) NaOMe, MeOH, **18a**, 73 % (over two steps); **18b,** 11 % (over two steps); g) *m*-CPBA, $NaHCO_3$, DCM, 74 %; h) $LiAlH_4$, THF (**16**, 20 %; **20**, 33 %).

protonate the hard C-3 oxygen, with consequent debenzoxylation and formation of the delocalized allylic oxycarbenium ion characteristic of the Ferrier rearrangement, that reacts with the alcohol to selectively afford the thermodinamically more stable anomer.[6] Nevertheless, the approach using a benzyl protected starting material is less appealing than the one starting from acetyl protected glycals, as an overall yield of 43 % is obtained for **22a,b** with low selectivity for the α-anomer.

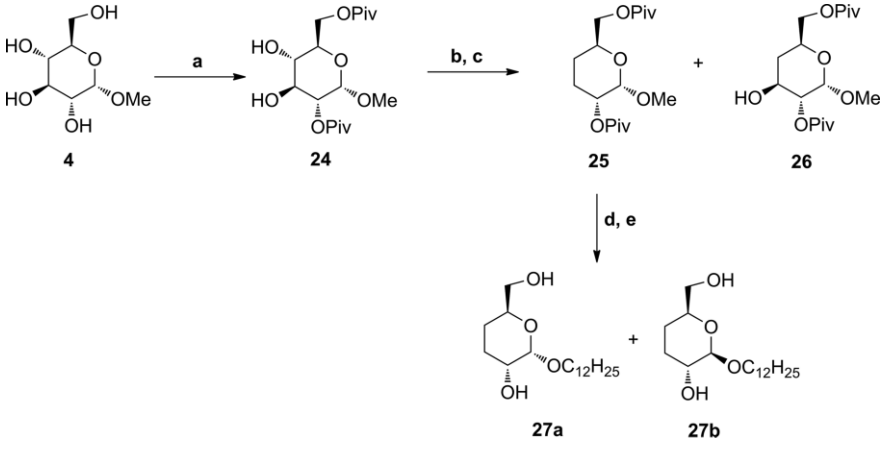


Scheme 3. Synthesis of dodecyl 2,3-dideoxy-D-*erythro*-hexopyranoside (**23**). a) $C_{12}H_{25}OH$, HY, DCE, 43 %; b) Et_3SiH 10 % Pd/C, 51 %.

Deoxygenation of positions 3 and 4 (Scheme 4) is effectively achieved by selectively protecting positions 2 and 6 with the pivaloyl group, triflation of the remaining free hydroxy groups and reaction with tetrabutylammonium borohydride. The methyl 3,4-dideoxy glycoside **25** is isolated in 29 % yield, with the concomitant formation of the 4-deoxy derivative **26** in 33 % yield. Reaction of **25** with dodecan-1-ol in the presence of Amberlyst 15 affords the dodecyl glycosides that, after deacylation, give the target molecules **27a** and **27b**.

Antimicrobial activity and cytotoxicity. Antimicrobial activity over three *B. anthracis* strains, *B. cereus* and *E. faecalis* is evaluated by the Müller-Hinton agar dilution method, according to CLSI guidelines (Table 1). Compound **1**, deoxygenated in positions 4 and 6, is the most active one, presenting a potent antimicrobial activity in all tested strains. The lack of activity of its beta-anomer **11** confirms, once again, the tendency already reported by us for β-hexopyranosides.[3,4]

Interestingly, when only position 4 is deoxygenated (compound **8a**), a fourfold decrease in activity is found, in line with previous findings.[4] This result can be rationalized as the hydroxy group at position 6 is more readily solvated by water molecules, making this glycoside less lipophilic, with a negative impact on its interaction with the phosphatidylethanolamine enriched phospholipid membranes. Apart from these observations, there is no clear tendency regarding the effect of the deoxygenated position by considering the 2-, 3- and 4-deoxy glycosides (compounds **8a**, **16** and **20**), all of them presenting the same MIC values. Dideoxygenated compound **23** presents



Scheme 4. Synthesis of dodecyl 3,4-dideoxy-D-*erythro*-hexopyranosides. a) PivCl, py, DCM, 65 %; b) Tf_2O, py, DCM, –10 °C; c) nBu_4NBH_4, THF, 29 % (over two steps); d) $C_{12}H_{25}OH$, Amberlyst15; e) KOH, H_2O:MeOH (**27**, 36 %; **28**, 15 %, over two steps).

Table 1. Antibacterial activity expressed in MIC values and cytotoxicity (IC_{50}).

Compound	MIC in μM					Cytotoxicity (IC_{50}) in μM	
	B. anthracis			*E. faecalis*	*B. cereus*	*Caco-2*	*Hep G2*
	Sterne	*pathog.*	*Ovine*				
1,[4] 4,6-dideoxy, α	12.6	12.6	12.6	12.6	12.6	50	>100
2,[4] 2,6-dideoxy, α	50	50	50	50	25	100	50
3,[3] 2-deoxy	386	12	12	12	386	50	n.d.
8a, 4-deoxy, Pyr	48	48	48	48	48	n.d.	n.d.
11, 4,6-dideoxy, β	>405	>405	>405	>405	>405	50	n.d.
15, 3-deoxy, Fur	96	96	96	96	96	100	n.d.
16, 3-deoxy, Pyr	48	48	48	48	48	50	100
20, 2-deoxy, Pyr	48	48	48	96	96	>50	n.d.
23, 2,3-dideoxy	50	50	50	50	50	100	100
27, 3,4-dideoxy	101	101	101	101	101	>50	n.d.
Ref.[a]	25	25	25	25	25	n.d.	n.d.

[a] Chloramphenicol was used as reference.

virtually the same antimicrobial activity against *B. anthracis* strains, while the 3,4-deoxy compound **27a** is the less active one of the group. It is also interesting to note that pyranoside **16** is active at 48 μM while its furanose analogue (**15**) is twice less active. The difficult structure-activity relationship underlying these results is indeed a well-known characteristic of membrane-targeting antimicrobial compounds.[7]

The cell viability of intestinal (Caco-2) and hepatic (HepG2) cell models was assessed by the MTT assay, after 48 h of incubation time. With the exception of compounds **1** and **3**, most compounds showed toxicity values in Caco2 cells of the same order of magnitude, or higher, than those exhibited for their bactericide activity. Only compounds **1**, the most active one, and the analogues **2**, **16** and **23** were selected to be tested in HepG2 cells. The IC_{50} of all tested compounds is 50 μM or above, with compounds **1**, **16** and **23** being the less toxic for intestinal cells. Compound **1** presented an IC_{50} four times its MIC value for Caco-2 cells, and more than eight times the MIC value for HepG2 cells making it the most promising lead for further development.

Conclusions

Aiming at recognizing the role of deoxygenation pattern for optimization of dodecyl glycoside antimicrobial activity, mono- and dideoxy dodecyl glycosides were successfully synthesized in moderate to good yields. The usefulness of Amberlyst 15 as glycosylation promoter is patent, particularly for the transacetalation of methyl glycosides (Scheme 2 and Scheme 4) to easily access the dodecyl glycosides. This heterogeneous catalyst, alternatively to the Lewis acids commonly used, is recovered, environmentally friendly, and affords stereoselectively the most active α-anomer. Its successful use with the free sugar avoids additional protection and deprotection steps required when other Lewis acid catalysts are applied, leading to the regioselective formation of hexofuranosides by a single reaction step, also an achievement within synthetic methodologies known for such structures. In addition, catalyst removal by filtration facilitates reaction work up and consequently the isolation of both the hexopyranoside/hexofuranoside isomers, that is much easier than when other catalysts are used. Deoxygenation carried out by triflation and reaction with tetrabutylammonium borohydride has proven as an efficient route for the synthesis of the 3-, 4-, 4,6- and 3,4- deoxygenated compounds.

Dodecyl 2-, 3-, 4-deoxy, and 2,3-, 3,4-, and 4,6-dideoxy glycosides were tested for their antimicrobial activity. As it is appanage of membrane-targeting antimicrobial compounds, the structure-activity relationship underlying the antimicrobial results was not so clear, as the impact of the deoxygenation position or the number of deoxygenated positions was not linear. The 2-deoxy-D-*arabino*-pyranoside shows a promising MIC value for *B. anthracis* pathogenic, *B. anthracis* ovine and *E. faecalis* but is not active for *B. cereus* and *B.anthracis* Sterne. Nevertheless, the configuration at C-3 is relevant for the bioactivity over these species, as a fourfold decrease in bioactivity, or higher is found when glycone configuration at C-3 is inverted or embodies a 3-deoxygenation. The 2,3 and 3,4-dideoxygenation pattern do not seem to improve bioactivity, while 4,6-dideoxygenation rises as the most promising structural feature, leading to compound **1,** active over all microbes tested, and presenting an IC_{50} four/eight times its MIC value for Caco-2 cells, and HepG2 cells, respectively.

Experimental Section

Chemistry. Starting materials and reagents were purchased from Sigma–Aldrich, Fluka and Acros. The solvents were dried prior to use with 4 Å or 3 Å (methanol) molecular sieves. The spectroscopic and physical data of these compounds are in agreement with those previously reported. TLC was carried out on aluminium sheets (20 cm × 20 cm) coated with 0.2 mm silica gel 60 F-254 (Merck) and detection was accomplished by spraying the plates with a solution of H_2SO_4 in ethanol (10 %) followed by heating at 120 °C. The compounds were purified by column chromatography (CC) using silica gel 60 (0.040–0.063 mm, Merck) or silica gel 60 (0.015–0.040 mm, Merck). Melting points were first obtained with a SMP3 Melting Point Apparatus, Stuart Scientific, Bibby. Optical rotations were measured with a Perkin–Elmer 343 polarimeter. Compound structural characterization was accessed by NMR and high-resolution

mass spectrometry (MS) analyses. Specific NMR assignments were determined by multidimensional and decoupling experiments. ^{1}H and ^{13}C NMR spectra for final compounds are provided in Supplementary Information (Figures S1 to S18). NMR spectra were recorded with a Bruker Avance 400 spectrometer at 298 K operating at 100.62 MHz for ^{13}C NMR and at 400.13 MHz for ^{1}H NMR spectroscopy. The solvents used were $CDCl_3$ with 0.03 % TMS and CD_3OD (Sigma–Aldrich). The chemical shifts are reported as δ (ppm) and the coupling constants (*J*) are given in Hz. High resolution ESI positive mode mass spectra were obtained on a QqTOF Impact II™ mass spectrometer (Bruker Daltonics) operating in the high-resolution mode. Samples were analyzed by flow injection analysis (FIA) using a isocratic gradient 50 A:50 B of 0.1 % formic acid in water (A) and 0.1 % of formic acid in acetonitrile (B), at a flow rate of 5 µL min^{-1} over 15 min. Calibration of the TOF analyzer was performed with a calibrant solution of sodium formate 10 mM. The full scan mass spectra were acquired over a mass range of 50–1000 *m/z* at a spectra rate of 0.2 Hz. Data was processed using Data Analysis 4.2 software.

Methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (5). To a solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside[8] (3 g, 10.6 mmol) in DMF (200 mL), NaH (60 % oil suspension, 2.84 g, 42.4 mmol, 4 equiv.) was carefully added at 0 °C and the reaction was stirred for 15 min. Then, benzyl bromide (5.1 mL, 42.4 mmol, 4 equiv.) was added and the reaction was stirred at room temperature overnight. The reaction was quenched by pouring it into cooled water (200 mL) and extracted with DCM (3 × 100 mL). Organic phases were combined, washed with saturated aqueous sodium hydrogen carbonate and dried with $MgSO_4$. After filtration and concentration under reduced pressure, the residue was purified by CC (hex→hex/EtOAc, 5:1), affording compound **5** as a white solid in 82 % yield (4.03 g). Physical and spectroscopic data were in agreement with this structure, previously reported in the literature.[9]

Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (6). To a solution of compound **5** (3.00 g, 6.49 mmol) in acetonitrile (60 mL) containing 4Å molecular sieves (ca. 200 mg), sodium cyanoborohydride (2.037 g, 32.4 mmol, 5 equiv.) was added. Then, molecular iodine (3.781 g, 14.9 mmol, 2.3 equiv.) was added portion wise over 1 h (each time iodine was added the solution became orange and only when the solution became white more iodine was added). After completion of the starting material (3 h), the reaction mixture was diluted with DCM (100 mL) and filtered through Celite. The filtered solution was washed with saturated aqueous sodium hydrogen carbonate and then water. Organic phases were combined and dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give a syrup purified by CC eluted with CyHex-EtOAc 4:1, affording compound **6** as a colorless oil in 77 % yield (2.32 g). Physical and spectroscopic data are fully in agreement with the assigned structure, that was previously reported in the literature.[10]

Methyl 2,3,6-tri-*O*-benzyl-4-deoxy-α-D-*xylo*-hexopyranoside (7). Compound **6** (2.30 g, 4.95 mmol) was dissolved in DCM (70 mL) and pyridine (0.9 mL, 11.39 mmol, 2.3 equiv.), and cooled to –10 °C, under N_2. Trifluoromethanesulfonic anhydride (1.92 mL, 11.39 mmol, 2.3 equiv.) was then added dropwise to the stirred solution, which was then warmed to 2 °C and stirred for 2 h 30 min. The reaction was quenched by addition of cool distilled water (100 mL), followed by extraction with DCM (2 × 100 mL). Organic phase was dried with $MgSO_4$, filtered and evaporated under reduced pressure, affording highly labile off-white powder composed by methyl 2,3,6-tri-*O*-benzyl-4-deoxy-4-trifluoromethanesulfonyl-α-D-glucopyranoside. The solid was dissolved in toluene (74 mL), and tetra-*n*-butylammonium borohydride (3.76 g, 14.85 mmol, 3 equiv.) was added. The reaction mixture was stirred at 85 °C for 2 h, cooled to room temperature and then poured into ice cold water (100 mL). After extraction with DCM (2 × 50 mL), the organic phase was washed with saturated aqueous sodium hydrogen carbonate (2 × 50 mL) and water (50 mL). Organic phases were combined and dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by CC eluted with hex/EtOAc, 10:1 to afford compound **7** as a colorless oil in 83 % yield (1.84 g). Physical and spectroscopic data were in agreement with those previously reported for this compound.[11]

Dodecyl 4-deoxy-D-*xylo*-hexopyranoside (8a,b). A solution of compound **7** (1.498 g, 3.34 mmol) in dodecan-1-ol (11.2 mL, 50 mmol, 15 equiv.), containing Amberlyst 15 beads (0.250 g) was stirred at 100 °C for 4.5 h. The solution was diluted with DCM, the resin beads were filtered off, and the solution was concentrated under reduced pressure. The residue was taken up in methanol (15 mL) and, after addition of Pd/C 10 % (50 mg) and inertization of the vessel with N_2, triethylsilane (1.8 mL, 21.26 mmol, 6.4 equiv.) was added dropwise. After 24 h, the catalyst was filtered off using Celite, the solvent was evaporated under reduced pressure, and the residue was purified by CC (Petrol. ether/EtOAC, 1:1 → EtOAc). The anomeric mixture **8a**,**b** (1.1:1 α/β) was obtained as a white solid, in 80 % yield (0.89 g). R_f (EtOAc/Tol, 3:1) = 0.20; **^{1}H NMR** (400.13 MHz, CD_3OH, 25 °C): δ = 4.80 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1α-H), 4.19 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, 1β-H), 3.91–3.80 (m, 3 H, 3α-H, 5α-H and 1′aβ-H), 3.71 (td, $^3J_{1'a,1'b}$= 9 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1′aα-H), 3.65–3.48 (m, 7 H, 3β-H, 5β-H, 6α-H, 6β-H, 1′bβ-H), 3.41 (td, 1 H, 1′bα-H), 3.32 (m, 1 H, 2α-H)*, 3.08 (t, $^3J_{1,2}$ = $^3J_{2,3}$ = 7.9 Hz, 1 H, 2β-H), 1.93 (br dd, 2 H, $^3J_{4ax,4eq}$= 12 Hz, $^3J_{4eq,5}$ = $^3J_{3,4eq}$= 5 Hz, 4_{eq}α-H, 4_{eq}β-H), 1.69–1.67 (m, 4 H, 2′α-H, 2′β-H), 1.42–1.25 (m, 38 H, 3′-H to 11′-H α and β, 4_{ax}α-H, 4_{ax}β-H), 0.92–0.88 (m, 6 H, 12′α-H, 12′β-H) ppm. **^{13}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 104.7 (C-1β), 100.7 (C-1α), 76.9 (C-2β), 75.6 (C-2α), 73.9, 72.3, 70.9, 70.0 (C-3, C-5, α and β), 69.1 (C-1′α), 68.9 (C-1′β), 65.7 (C-6α), 65.6 (C-6β), 36.6 (C-4α, C-4β), 33.2, 30.9, 30.9, 30.7, 30.6, 27.4, 27.2, 23.8 (C-2′ to C-11′ α and β), 14.6 (C-12′ α and β) ppm. *Signal under MeOH signal. **HRMS**: Calcd. [$C_{18}H_{36}NaO_5$] 335.2455, found 335.2451 (error 1.0 ppm).

Dodecyl 4-deoxy-α-D-*xylo*-hexopyranoside (8a). An aliquote of the anomeric mixture **8a**,**b** was further purified by CC with $CHCl_3$:EtOH 95:5, to afford the pure alfa-anomer (**8a**) for characterization and biological evaluation. R_f ($CHCl_3$:EtOH 9:1) = 0.3; m.p. = 79.6–80.7 °C; $[\alpha]_D^{20}$ = 71° (*c*1, MeOH). **^{1}H NMR** (400.13 MHz, CD_3OH, 25 °C): δ = 4.80 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 3.89–3.80 (m, 2 H, 3-H, 5-H), 3.71 (td, $^3J_{1'a,1'b}$= 9 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1′a-H), 3.52 (br d, $^3J_{5,6}$ = 5 Hz, 2 H, 6a,b-H), 3.41 (td, 1 H, 1′b-H), 3.30 (1H, 2-H)*, 1.92 (ddd, $^3J_{4ax,4eq}$ = 12 Hz, $^3J_{4eq,5}$ = 2, $^3J_{3,4eq}$ = 5 Hz, 1 H, 4_{eq-H}), 1.71–1.55 (m, 2 H, 2′-H), 1.48–1.23 (m, 19 H, 3′-H to 11′-H, and 4_{ax}-H), 0.92 (t, 3 H, 12′-H) ppm. **^{13}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 100.7 (C-1), 75.5 (C-2), 73.8, 69.9 (C-3, C-5), 69.0 (C-1′), 65.7 (C-6), 36.5 (C-4), 33.1, 30.8, 30.7, 30.6, 30.5, 27.4, 23.7 (C-2′ to C-11′), 14.5 (C-12′) ppm. *Signal partially under MeOH signal. **HRMS**: Calcd. [$C_{18}H_{36}NaO_5$] 335.2455, found 335.2444 (error 3.0 ppm).

Dodecyl 4,6-dideoxy-α/β-D-*xylo*-hexopyranoside (1, 11). The anomeric mixture **8a,b** (0.3176 g, 0.955 mmol) was dissolved in DCM (10 mL) and pyridine (0.12 mL, 1.43 mmol, 1.5 equiv.), and cooled to –10 °C, under N_2. Trifluoromethanesulfonic anhydride (0.24 mL, 1.43 mmol, 1.5 equiv.) was added dropwise to the stirring solution, which was then warmed to 2 °C and stirred for 1 h. The reaction was quenched by addition of 20 mL of cool distilled water, followed by extraction with DCM (2 × 20 mL). The organic phase was dried with $MgSO_4$, filtered and evaporated under reduced pres-

sure at 25 °C, affording a syrup. This intermediate triflate was dissolved in THF (8.3 mL), and a 2 M $LiAlH_4$ solution in THF (1.67 mL, 3.34 mmol, 3.5 equiv.) was added dropwise at 0 °C. After stirring 1 h at room temperature, the reaction was cooled again to 0 °C and the aluminium salts were removed by slow addition of water (0.3 mL), aqueous NaOH 15 % (0.9 mL) and water (0.9 mL) to give a mixture kept whilst stirring for 15 min at room temperature. Addition of $MgSO_4$ resulted in a suspension, and after filtration of the solids, the solution was concentrated under reduced pressure to give a syrup composed by an inseparable anomeric mixture of dodecyl 4,6-dideoxy-D-*xylo*-hexopyranoside, which was dissolved in pyridine (4 mL), and Ac_2O (2 mL) followed by a spatula tip of DMAP. The reaction was stirred at room temperature overnight. The fully acetylated α and β glycosides could be distinguished in the TLC plate (hex/EtOAc, 5:1). After co-evaporation of pyridine with toluene, the anomers were purified by column chromatography (hex/EtOAc, 25:1) to afford the dodecyl 2,3-di-*O*-acetyl-4,6-dideoxy-α-D-*xylo*-hexopyranoside (**9**, 116 mg, 30 % yield) and dodecyl 2,3-di-*O*-acetyl-4,6-dideoxy-β-D-*xylo*-hexopyranoside (**10**, 42 mg, 11 % yield). The acetylated compound (**9** or **10**) was dissolved in methanol (100mg/mL), and a 1M solution of NaOMe in methanol (0.1 mL per 0.100 mg of substrate) was added. The reaction mixture was stirred for 2 h at room temperature. Neutralization with Amberlite IR-120, filtration and evaporation of the solvent, afforded the deacetylated compounds **1** and **11** in quantitative yield.

Dodecyl 2,3-di-*O*-acetyl-4,6-dideoxy-α-D-*xylo*-hexopyranoside (9). Syrup. R_f (hex/EtOAc, 5:1) = 0.50; **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 5.25 (ddd, $^3J_{2,3}$ = 10 Hz, $^3J_{3,4ax}$ = 11 Hz, $^3J_{3,4eq}$ = 5 Hz, 1 H, 3-H), 4.97 (d, $^3J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 4.80 (dd, 1 H, 2-H), 4.05–3.95 (m, 1 H, 5-H), 3.65 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1'a-H), 3.36 (td, $^3J_{1'b,2'}$ = 7 Hz, 1 H, 1'b-H), 2.18 (br dd, $^3J_{3,4eq}$= 5 Hz, $^3J_{4eq,5}$ = 1 Hz, 1 H, 4eq-H), 2.06 (s, 3 H, -OAc), 2.02 (s, 3 H, -OAc), 1.60–1.52 (m, 2 H, 2'-H), 1.41 (q, $^3J_{3,4ax}$ = $^3J_{4,5}$ = $^3J_{4eq,4ax}$ = 11 Hz, 1 H, 4ax-H), 1.35–1.21 (m, 18 H, 3'-H to 11'-H), 1.18 (d, $^3J_{5,6}$ = 6 Hz, 3 H, 6-H), 0.87 (t, $^3J_{11',12'}$ = 6 Hz, 3 H, 12'-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 170.5 (C=O, OAc), 170.3 (C=O, OAc), 96.3 (C-1), 72.2 (C-2), 68.2 (C-3), 68.0 (C-1'), 63.0 (C-5), 38.2 (C-4), 31.9, 29.7, 29.6, 29.4, 29.3, 26.1, 22.7 (C-2' to C-11'), 21.1 (CH_3, OAc), 20.9 (CH_3, OAc), 20.6 (C-6), 14.1 (C-12') ppm.

Dodecyl 2,3-di-*O*-acetyl-4,6-di-deoxy-β-D-*xylo*-hexopyranoside (10). Colorless oil; R_f (hex/EtOAc, 5:1) = 0.39; **^{1}H NMR** (400.13 MHz, CD_3OH, 25 °C): δ = 4.96 (ddd, $^3J_{2,3}$ = 10 Hz, $^3J_{3,4ax}$ = 10 Hz, $^3J_{3,4eq}$ = 5 Hz, 1 H, 3-H), 4.85 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 8 Hz, 1 H, 2-H), 4.35 (d, $^3J_{1,2}$ = 8 Hz, 1 H, 1-H), 3.85 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1'a-H), 3.68–3.58 (m, 1 H, 5-H), 3.45 (td, 1 H, 1'b-H), 2.12–2.06 (m, 1 H, 4eq-H), 1.71–1.42 (m, 5 H, 2'-H, 3'-H, 4ax-H), 1.41–1.17 (m, 19 H, 4'-H to 11'-H and 6-H), 0.86 (t, $^3J_{11',12'}$ = 7 Hz, 3 H, 12'-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 170.1 (C=O, OAc), 169.8 (C=O, OAc), 98.8 (C-1), 72.6 (C-2), 71.2 (C-3), 69.8 (C-1'), 67.7 (C-5), 37.9 (C-4), 31.9, 29.7, 29.6, 29.5, 29.4, 25.9, 22.7 (C-2' to C-11'), 21.0 (CH_3, OAc), 20.9 (CH_3, OAc), 20.7 (C-6), 14.1 (C-12') ppm.

Dodecyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside (1). Obtained from compound **9** (0.099g, 0.25 mmol), as a white solid in 96 % yield (0.076 g). R_f (tol/EtOAc, 2:3) = 0.31; M.p. = 34.3–36.0 °C; $[\alpha]_D^{20}$ = +103° (*c*1, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, CD_3OH, 25 °C): δ = 4.70 (d, $^3J_{1,2}$ = 3.4 Hz, 1H, 1-H), 3.90 (m, $^3J_{5,6}$ = 6 Hz, $^3J_{4eq,5}$ = 2 Hz, 1H, 5-H), 3.77 (qd, $^3J_{2,3}$ = $^3J_{3,4x}$ = 10 Hz, $^3J_{3,4eq}$ = 5 Hz, 1 H, 3-H), 3.62 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1'a-H), 3.40 (td, $^3J_{1'b,2'}$ = 6 Hz, $^3J_{1'b,2'}$ = 7 Hz, 1 H, 1'b-H), 3.24 (dd, $^3J_{2,3}$ = 9 Hz, 1 H, 2-H), 1.91 (ddd, $^3J_{4ax,4eq}$ = 12 Hz, 1 H, 4_{eq}-H), 1.65–1.51 (m, 2 H, 2'-H), 1.40–1.18 (m, 19 H, 3'-H to 11'-H and 4ax-H), 1.13 (d, $^3J_{5,6}$ = 6 Hz, 3 H, 6-H), 0.87 (br t, $^3J_{11',12'}$ = 6 Hz, 3 H, 12'-H) ppm. **^{13}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 100.8 (C-1), 75.5 (C-2), 69.1, 68.9 (C-1' and C-3), 65.2 (C-5), 42.3 (C-4), 33.1, 30.8, 30.7, 30.6, 30.5, 27.4, 23.8 (C-2' to C-11'), 21.2 (C-6), 14.5 (C-12') ppm. **HRMS**: Calcd. $[C_{18}H_{36}NaO_4]$ 339.2506, found 339.2509 (error –1.1 ppm).

Dodecyl 4,6-dideoxy-β-D-*xylo*-hexopyranoside (11). Obtained from compound **10** (0.030g, 0.075 mmol), as a white solid in 94 % yield (0.022 g). R_f (tol/EtOAc, 2:3) = 0.31; M.p. = 48.2–50.7 °C; $[\alpha]_D^{20}$ = –30° (*c*0.6, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, CD_3OH, 25 °C): δ = 4.12 (d, $^3J_{1,2}$ = 7.9 Hz, 1 H, 1-H), 3.78 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, H 1, 1'a-H), 3.60–3.44 (m, 3 H, 1'b-H, 3-H and 5-H), 3.01 (t, $^3J_{1,2}$ = $^3J_{2,3}$ = 8 Hz, 1 H, 2-H), 1.89 (ddd, $^3J_{4ax,4eq}$ = 13 Hz, $^3J_{3,4eq}$ = 2 Hz, 1 H, H-4_{eq}), 1.58 (m, $^3J_{1'a,2'}$ = $^3J_{2'a,3'}$ = 7 Hz, 2 H, H-2'), 1.39–1.21 18 (m, 19 H, 3'-H to 11'-H and 4ax-H), 1.13 (d, $^3J_{5,6}$ = 6 Hz, 3 H, H-6), 0.87 (br t, $^3J_{11',12'}$ = 6 Hz, 3 H, 12'-H) ppm. **^{13}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 104.6 (C-1), 76.8 (C-2), 72.2 (C-3), 70–9 (C-1'), 69.1 (C-5), 42.1 (C-4), 33.1, 30.9, 30.8, 30.6, 30.5, 27.1, 23.8 (C-2' to C-11'), 21.3 (C-6), 14.5 (C-12') ppm. **HRMS**: Calcd. $[C_{18}H_{36}NaO_4]$ 339.2506; Exp. 339.2495 (error 3.3 ppm).

1,2:5,6-Di-*O*-isopropylidene-3-deoxy-α-D-*ribo*-hexofuranose (13). Triflic anhydride (1.3 mL, 7.68 mmol, 2 equiv.) was added dropwise to a stirring solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1.00g, 3.84 mmol) in DCM (30 mL) and pyridine (0.62 mL, 7.68 mmol, 2 equiv.), at –10 °C under N_2. The reaction was stirred for 15 min, after which complete conversion of the starting material into the triflate derivative occurred. The reaction was poured into 50 mL of ice cold water and the organic phase was separated. The aqueous phase was further extracted with DCM (2 × 50 mL). Organic phases were combined, dried with $MgSO_4$ and evaporated under reduced pressure, affording 1,2:5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-*ribo*-hexofuranose as a colorless oil in 82 % yield. R_f (hex/EtOAC, 2:1) = 0.78, **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 5.98 (d, $^3J_{1,2}$ = 5 Hz, 1 H, 1-H), 5.36 (br s, 1 H, 3-H), 4.76 (d, 1 H, 2-H), 4.22–4.13 (m, 3 H, 4-H, 5-H, 6a-H), 3.97 (dd, $^3J_{6a,6b}$ = 9 Hz, $^3J_{5,6b}$ = 3 Hz, 1 H, 6b-H), 1.52 (s, 3 H, -CH_3 isoprop.), 1.42 (s, 3 H, -CH_3 isoprop.), 1.34 (s, 3 H, -CH_3 isoprop.), 1.33 (s, 3 H, -CH_3 isoprop.) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 113.1 (Cq isoprop.), 109.8 (Cq isoprop.), 105.0 (C-1), 88.1 (C-2),83.2 (C-3), 79.9 (C-4), 71.7 (C-5), 67.6 (C-6), 26.8, 26.5, 26.2, 24.8 (-CH_3 isoprop.) ppm.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-triflyl-α-D-*ribo*-hexofuranose (1.85 g, 4.74 mmol) was dissolved in dried toluene (100 mL) and nBu_4NBH_4 (2.4 g, 9.47 mmol, 2 equiv.) was added in one portion. The reaction mixture was refluxed under N_2 for 4 h and quenched by pouring the solution into ice cold water (40 mL). The organic phase was extracted with DCM (2 × 50 mL) and washed with a saturated sodium hydrogen carbonate (50 mL) and water (50 mL). The organic phase was dried with $MgSO_4$ and evaporated under reduced pressure. The resulting residue was purified by column chromatography, eluted with hex/EtOAc, 9:1, affording compound **13** as a colorless oil in 54 % yield (0.624 g). R_f (Hex/EtOAC, 4:1) = 0.31; $[\alpha]_D^{20}$ = –5° (*c*1, $CHCl_3$); **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 5.82 (d, $^3J_{1,2}$ = 3 Hz, 1 H, 1-H), 4.76 (br t, $^3J_{2,3b}$ = 4, 1 H, 2-H), 4.19–4.09 (m, 3 H, 4-H, 5-H, 6a-H), 3.82 (dd, $^3J_{6a,6b}$ = 8 Hz, $^3J_{5,6b}$ = 5 Hz, 1 H, 6b-H), 2.19 (dd, $^3J_{3a,3b}$ = 14 Hz, $^3J_{3a,4}$ = 3 Hz, 1 H, 3a.H), 1.77 (ddd, $^3J_{3b,4}$ = 5 Hz, 1 H, 3b-H), 1.52 (s, 3 H, -CH_3 isoprop.), 1.43 (s, 3 H, -CH_3 isoprop.), 1.36 (s, 3 H, -CH_3 isoprop.), 1.32 (s, 3 H, -CH_3 isoprop.) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 111.3 (Cq isoprop.), 109.6 (Cq isoprop.), 105.6 (C-1), 80.4 (C-2), 78.6 (C-4, C-5), 67.2 (C-6), 35.2 (C-3) 26.8, 26.5, 26.2, 24.8 (-CH_3 isoprop.) ppm. **HRMS**: Calcd. $[C_{12}H_{21}O_5]$ 245.1384, found 245.1392 (error 3.3 ppm).

3-Deoxy-D-*ribo*-hexopyranose (14). Compound **13** (1.00 g, 4.09 mmol), was dissolved in aqueous trifluoroacetic acid 80 % (7 mL) and stirred at 40 °C for 2 h. Co-evaporation of the acid with

toluene gave **14** as a colorless oil in quantitative yield (α/β, 0.8:1) (0.67 g). R_f (DCM/EtOH, 9:1) = 0.15; **^{1}H NMR** (400.13 MHz, CD_3OD, 25 °C): δ = 4.95 (d, $^3J_{1,2}$ = 3 Hz, 1 H, 1α-H), 4.33 (d, $^3J_{1,2}$ = 8 Hz, 1 H, 1β-H), 3.77–3.66 (m, 1 H, 6aβ-H), 3.59–3.50 (m, 4 H, 2α-H, 6bβ-H, 6aα-H, 5β-H), 3.49–3.36 (m, 3 H, 4α-H, 6bα-H, 4β-H), 3.27–3.13 (m, 2 H, 5α-H, 2β-H), 2.20 (td, $^3J_{2,3eq}$ = $^3J_{3eq,4}$ = 5 Hz, $^3J_{3ax,3eq}$ = 12 Hz, 1 H, 3_{eq}β-H), 1.99–1.92 (m, 1 H, 3_{eq}α-H), 1.72 (q, $^3J_{2,3ax}$ = $^3J_{3ax,4}$ = $^3J_{3ax,3eq}$ = 12 Hz, 1 H, 3_{ax}β-H), 1.39 (q, 1H, $^3J_{2,3ax}$ = $J_{3ax,4}$ = $J_{3ax,3eq}$ = 12 Hz, 1 H, 3_{ax}α-H) ppm. **^{13}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 100.1 (C-1β), 92.6 (C-1α), 81.7 (C-β), 80.7, 76.8 (C-4α, C-4β), 73.7 (C-5 α), 70.4 (C-2β), 66.2 (C-2α), 65.1 (C-6α), 62.8 (C-6β), 40.5 (C-3β), 36.1 (C-3α) ppm. **HRMS**: Calcd. [$C_6H_{12}NaO_5$] 187.0577, found 187.0574 (error –1.6 ppm).

Fischer glycosylation procedure. Compound **14** (0.050g, 0.305 mmol) and Amberlyst 15 (50 mg/300 mg substrate) were dissolved in dodecan-1-ol (0.851 mL, 0.457 mmol, 15 equiv.) and the solution was stirred for 5 h at 100 °C. Reaction products were isolated by CC eluted with a gradient from dichloromethane to dichlotomethane/ethanol, 10:1. Compound **15** was isolated in 28 % yield, as a colorless oil (28.4 mg), while compound **16** was isolated in 8 % yield, as a white solid (8.1 mg). Both beta anomers were detected in the TLC as traces and were not isolated.

Dodecyl 3-deoxy-α-D-*ribo*-hexofuranoside (15). R_f (DCM/MeOH, 12:1) = 0.29; $[\alpha]_D^{20}$ = –50° (*c*0.1, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, CD_3OD, 25 °C): δ = 4.83 (s, 1 H, H-1), 4.22 (q, $^3J_{3a,4}$ = $^3J_{3b,4}$ = $^3J_{4,5}$ = 7 Hz, 1 H, H-4), 4.13 (d, $^3J_{2,3a}$ = 4 Hz, 1 H, 2-H), 3.73 (dd, $^3J_{5,6a}$ = 3Hz, $^3J_{6a,6b}$ = 12 Hz, 1 H, 6a-H), 3.65 (br td, $^3J_{1'a,1'b}$ = 9 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1′a-H), 3.55 (dd, $^3J_{5,6b}$ = 6 Hz, 1 H, 6b-H), 3.46 (ddd, 1 H, 5-H), 3.36 (td, $^3J_{1'b,2'}$ = 7 Hz, 1 H, 1′b-H),

2.07 (ddd, 1 H, 3a-H), 1.97 (dd, $^3J_{3b,4}$ = 7 Hz, $^3J_{3a,3b}$ = 13 Hz, 1 H, 3b-H), 1.58–1.49 (m, 2 H, 2′-H), 1.39–1.22 (m, 18 H, 3′-H to 11′-H), 0.90 (t, $^3J_{11',12'}$ = 6Hz, 3 H, 12′-H) ppm. **^{1}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 109.7 (C-1), 80.7 (C-4), 76.9 (C-5), 76.5 (C-2), 68.4 (C-1′), 65.2 (C-6), 36.0 (C-3), 33.1, 30.8, 30.7, 30.6, 30.5, 27.3, 23.7 (C-2' to C-11′), 14.5 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{36}NaO_4$] 335.2455, found 335.2454 (error 0.3 ppm).

Dodecyl 3-deoxy-α-D-*ribo*-hexopyranoside (16). R_f (DCM/MeOH, 12:1) = 0.31; m.p. = 94.0–95.0 °C; $[\alpha]_D^{20}$ = +83° (*c*0.3, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, CD_3OD, 25 °C): δ = 4.64 (d, $^3J_{1,2}$ = 3 Hz, 1 H, 1-H), 4.59 (s, 1 H, OH), 3.80–3.68 (m, 2 H, 1′a-H, 6a-H), 3.64–3.54 (m, 2 H, 2-H, 6b-H), 3.50–3.39 (m, 3 H, 1′b-H, 4-H and 5-H), 2.01 (td, $^3J_{2,3eq}$ = $^3J_{3eq,4}$ = 4 Hz, $^3J_{3e,3ax}$ = 11 Hz, 1 H, 3eq-H), 1.76 (q, $^3J_{2,3ax}$ = $^3J_{3ax,4}$ = $^3J_{3e,3ax}$ = 11 Hz, 1 H, 3ax-H), 1.67–1.54 (m, 2 H, 2′-H), 1.45–1.20 (m, 18 H, 3′-H to 11′-H), 0.87 (t, 3 H, $^3J_{11',12'}$ = 6 Hz, 1 H, 12′-H) ppm. **^{1}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 98.9 (C-1), 74.4 (C-4), 68.8 (C-1′), 68.5 (C-2), 66.2 (C-5), 62.7 (C-6), 36.9 (C-3), 33.1, 30.8, 30.7, 30.5, 27.4, 23.8 (C-2′ to C-11′), 14.5 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{36}NaO_5$] 355.2455, found 355.2449 (error 1.6 ppm).

Dodecyl 2,3-dideoxy-α,β-D-*erythro*-hex-2-enopyranosides (18a,b). To a solution of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (2.0 g, 7.35 mmol) in dichloromethane (60 mL), dodecan-1-ol (1.81 mL, 8.08 mmol, 1.1 equiv.) and BF_3•Et_2O (0.05 mL, 0.37 mmol, 0.05 equiv.) were added. After 2 h at room temperature, the reaction, which had turned blue, was washed twice with $NaHCO_3$ (2 × 100 mL) and with brine (100 mL). The organic phase was dried with anhydrous $MgSO_4$, which was filtered off, and concentrated under reduced pressure. The resulting residue was dissolved in methanol (25 mL) and, after addition of a 1M solution of NaOMe in MeOH (0.6 mL), the reaction stirred for 1.5 h at room temperature. Neutralization with Amberlite IR-120, filtration and evaporation of the solvent gave a residue that was purified by CC eluted with hex/EtOAc, 2:1, affording compound **18a** as a white solid in 73 % yield (1.69 g), along with the beta anomer **18b** as a colorless oil in 11 % yield (0.025 g).

Dodecyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (18a). R_f (hex/EtOAc, 1:1) = 0.45; m.p. = 68.6–69.6 °C; $[\alpha]_D^{20}$ = +45° (*c*0.3, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 5.87 (br d, $^3J_{2,3}$ = 10 Hz, 1 H, 3-H), 5.69 (td, $^3J_{1,2}$ = 2 Hz, 1 H, 2-H), 4.93 (br s, 1 H, 1-H), 3.99 (dd, 1H, $^3J_{3,4}$ = 1 Hz, $^3J_{4,5}$ = 9 Hz, 1 H, 4-H), 3.83–3.74 (m, 2 H, 6a-H and 1′a-H), 3.70–3.57 (m, 2 H, 5-H and 6b-H), 3.44 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'b,2'}$ = 6 Hz, 1 H, 1′b-H),1.60–1.51 (m, 2 H, 2′-H), 1.39–1.20 (m, 18 H, 3′-H to 11′-H), 0.88 (t, $^3J_{11',12'}$ = 6 Hz, 3 H, 12′-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 134.6 (C-3), 127.3 (C-2), 95.5 (C-1), 73.6 (C-5), 69.5 (C-1′), 64.2 (C-4), 62.7 (C-6), 33.1, 30.9, 30.8, 30.6, 30.5, 27.4, 23.8 (C-2′ to C-11′), 14.5 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{34}NaO_4$] 337.2349, found 337.2348 (error 0.5 ppm).

Dodecyl 2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside (18b). R_f (hex/EtOAc, 1:1) = 0.33; $[\alpha]_D^{20}$ = +8° (*c*1, MeOH); **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 6.02 (br d, $^3J_{2,3}$ = 10 Hz, 1 H, 3-H), 5.78 (br d, 1 H, 2-H), 5.14 (br s, 1 H, 1-H), 4.20 (br d, $^3J_{4,5}$ = 5 Hz, 1 H, 4-H), 3.90–3.75 (m, 3 H, 6a-H, 6b-H and 1′a-H), 3.68 (ddd, $^3J_{5,6a}$ = 2 Hz, $^3J_{5,6b}$ = 6 Hz, 1 H, H-5), 3.51 (td, $^3J_{1'a,1'b}$ = 9 Hz, $^3J_{1'b,2}$ = 7 Hz, 1 H, 1′b-H), 2.88 (br s, 2 H, OH), 1.64–1.54 (m, 2 H, 2′-H), 1.38–1.18 (m, 18 H, 3′-H to 11′-H), 0.88 (t, $^3J_{11',12'}$ = 6 Hz, 3 H, 12′-H) ppm **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 132.0 (C-3), 128.1 (C-2), 96.3 (C-1), 78.2 (C-5), 68.7 (C-1′), 63.3, 63.2 (C-4 and C6), 31.9, 29.7, 29.6, 29.5, 29.4, 26.0, 22.7 (C-2′ to C-11′), 14.1 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{34}NaO_4$] 337.2349, found 337.2353 (error –1.1 ppm).

Dodecyl 2,3-anhydro-α-D-*allo*-hexopyranoside (19). Sodium hydrogen carbonate (0.033g, 0.40 mmol, 2 equiv.) and *m*-CPBA (0.069g, 0.40 mmol, 2 equiv.) were added to a stirring solution of 2,3-unsaturated compound **18a** (0.063g, 0.20 mmol) in DCM (2 mL). The solution was stirred vigorously at room temperature for 3 days. The reaction mixture was diluted with DCM (10 mL), washed with saturated aqueous $NaHCO_3$ (2 × 25 mL), and saturated aqueous $Na_2S_2O_3$ (2 × 25 mL). The organic phase was dried with $MgSO_4$, filtered and evaporated, to give a residue, which was purified by CC eluted with cyHex/EtOAc, 1:1. Compound **19** was isolated in 74 % yield (0.043 g), based on reacted starting material, recovered in 12 % yield. R_f (hex./EtOAc, 1:2) = 0.23; m.p.= 91.2–94.0 °C; $[\alpha]_D^{20}$ = +40° (*c*0.1, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, CD_3OD, 25 °C): δ = 4.96 (d, $^3J_{1,2}$ = 3 Hz, 1 H, 1-H), 4.60 (br s, 1 H, OH), 3.83–3.68 (m, 3 H, 6a-H, 1′a-H, 5-H), 3.63–3.56 (m, 2 H, 6b-H, 4-H), 3.50–3.43 (m, 2 H, 1′b-H, 2-H), 3.35 (br dd, $^3J_{2,3}$ = 4.0 Hz, $^3J_{3,4}$ = 1.5 Hz, 1 H, 3-H), 1.63–1.54 (m, 2 H, 2′-H), 1.40–1.22 (m, 18 H, 3′-H to 11′-H), 0.87 (t, $^3J_{11',12'}$ = 7 Hz, 3 H, 12′-H) ppm. The coupling constants are in agreement with those registered for an acetylated analogue in the literature[12] **^{1}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 94.9 (C-1), 70.9 (C-4), 69.2 (C-1′), 66.4 (C-5), 62.4 (C-6), 56.2 (C-2), 55.2(C-3), 33.1, 30.8, 30.7, 30.6, 30.5, 27.3, 23.8 (C-2′ to C-11′), 14.5 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{34}NaO_5$] 353.2298, found 353.2308 (error –2.7 ppm).

Dodecyl 3-deoxy-α-D-*ribo*-hexopyranoside (16) and **dodecyl 2-deoxy-α-D-*ribo*-hexopyranoside (20).** To a solution of epoxide **19** (0.080g, 0.242 mmol) in THF (2 mL), a 2M solution of LiAlH4 in THF (0.24 mL, 0.484 mmol, 2 equiv.) was added dropwise, at 0 °C. After stirring for 24 h at room temperature, the reaction was cooled to 0 °C and the aluminium salts were removed by addition of water (0.2 mL), then aqueous NaOH 15 % (0.6 mL), then water (0.6 mL), and stirring for 15 min at room temperature. $MgSO_4$ was added to the resulting suspension and, after filtration of the solids, the solution was concentrated under reduced pressure to give a syrup, puri-

fied by CC eluted with hex/EtOAc, 1:3, to give both 3-deoxy glycoside and **16** and 2-deoxy glycoside **20** in 20 % yield (0.0161 g) and 33 % yield (0.0266 g), respectively, both as white solids.

Dodecyl 3-deoxy-α-D-*ribo*-hexopyranoside (16). White solid; R_f (hex./EtOAc, 1:4) = 0.35; Spectroscopic characterization is in full agreement with the product obtained by Fischer glycosylation (above).

Dodecyl 2-deoxy-α-D-*ribo*-hexopyranoside (20). R_f (hex./EtOAc, 1:4) = 0.54; m.p. = 51.6–52.8 °C; $[\alpha]_D^{20}$ = +13° (*c*0.5, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, CD_3OD, 25 °C): δ = 4.87 (1 H, 1-H, under MeOH signal), 4.60 (s, 1 H, OH), 3.91 (br d, $^3J_{2,3}$ = 3 Hz, 1 H, 3-H), 3.85–3.60 (m, 4 H, 1′a-H, 5-H, 6-H), 3.44 (dd, $^3J_{3,4}$ = 2 Hz, $^3J_{4,5}$ = 10 Hz, 1 H, 4-H), 3.36 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'b,2'}$ = 6 Hz, 1 H, 1′b-H), 2.02 (ddd, $^3J_{1,2eq}$ = 1 Hz, $^3J_{2eq,3}$ = 3Hz, $^3J_{2ax,2eq}$ = 14 Hz, 1 H, 2eq-H), 1.89 (td, $^3J_{2ax,3}$ = $^3J_{1,2ax}$ = 3 Hz, 2ax-H), 1.66–1.50 (m, 2 H, 2′-H), 1.40-1.20 (m, 18 H, 3′-H to 11′-H), 0.87 (t, $^3J_{11',12'}$ = 7 Hz, 1 H, 12′-H) ppm. **^{1}C NMR** (100.62 MHz, CD_3OD, 25 °C): δ = 98.3 (C-1), 70.0 (C-4), 69.0 (C-3), 68–9 (C-1′), 68.5 (C-5), 63.0 (C-6), 36.2 (C-2), 33.1, 30.8, 30.7, 30.6, 30.5, 27.4, 23.8 (C-2′ to C-11′), 14.5 (C-12′) ppm. **HRMS**: Calcd. $[C_{18}H_{36}NaO_5]$ 335.2455, found 335.2450 (error 1.3 ppm).

Dodecyl 4,6-di-*O*-benzyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosides (22a,b). To a solution of 3,4,6-tri-*O*-benzyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (0.500 g, 1.2 mmol) in dichloroethane (5 mL), dodecan-1-ol (0.559g, 3 mmol, 2.5 equiv.) and zeolyte HY (0.192g, pre-activated to 140 °C) were added. The reaction was heated to 100 °C under microwave irradiation (200 W) in a closed vessel microwave reactor for 30 min. The solution was then diluted in dichloroethane, filtered and concentrated. The residue was purified by CC eluted with Hex/EtOAc, 25:1, affording compounds **22a** and **22b** in 29 % (0.172 g) and 14 % yield (0.083 g), respectively, both as colorless oils.

Dodecyl 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (22a). R_f (hex/EtOAc, 8:1)= 0.5; $[\alpha]_D^{20}$ = +58° (*c*1, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 7.41–7.24 (m, 10 H, CH_2*Ph*), 6.09 (d, $^3J_{2,3}$ = 10 Hz, 1 H, 3-H), 5.80 (br d, 1 H, 2-H), 5.04 (br s, 1 H, 1-H), 4.72–4.44 (m, 4 H, *CH*$_2$Ph), 4.20 (d, $^3J_{4,5}$ = 9Hz, 1 H, 4-H), 4.02–3.96 (m, 1 H, 5-H), 3.83–3.69 (m, 3 H, 6-H, 1′a-H), 3.50 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1′b-H), 1.68–1.54 (m, 2 H, 2′-H), 1.40–1.20 (m, 18 H, 3′-H to 11′-H), 0.91 (t, $^3J_{11',12'}$ = 7 Hz, 3 H, 12′-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 138.2, 138.1 (Cq, Ph), 130.5 (C-3), 128.4, 128.3, 127.9, 127.8, 127.7, 127.6 (CH, Ph), 126.7 (C-2), 94.6 (C-1), 73.3, 71.0 (*C*H$_2$Ph), 70.3 (C-4), 69.1 (C-5), 68.9 (C-6), 68.7 (C-1′), 31.9, 29.8, 29.7, 29.6, 29.4, 29.3, 26.2, 22.7 (C-2′ to C11′), 14.1 (C-12′) ppm. **HRMS**: Calcd. $[C_{32}H_{46}NaO_4]$ 517.3291, found 517.3288 (error –0.4 ppm).

Dodecyl 4,6-di-*O*-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside (22b). R_f (hex./EtOAc, 8:1) = 0.49; **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = *δ* 7.39–7.20 (m, 10 H, CH_2*Ph*), 6.06 (d, $^3J_{2,3}$ = 10 Hz, 1 H, 3-H), 5.77 (br td, $^3J_{1,2}$ = 2 Hz, 1 H, 2-H), 5.01 (br s, 1 H, H-1), 4.67–4.42 (m, 4 H, *CH*$_2$Ph), 4.17 (d, $^3J_{4,5}$ = 9Hz, 1 H, 4-H), 3.98–3.93 (m, 1 H, 5-H), 3.83–3.66 (m, 3 H, 6-H, 1′a-H), 3.47 (td, $^3J_{1'a,1'b}$ = 9 Hz, $^3J_{1'a,2'}$ = 6 Hz, 1 H, 1′b-H), 1.61–1.54 (m, 2 H, 2′-H), 1.35–1.20 (m, 18 H, 3′-H to 11′-H), 0.88 (t, $^3J_{11',12'}$ = 7 Hz, 3 H, 12′-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 138.3, 137.9 (Cq, Ph), 129.2 (C-3), 128.4, 128.3, 127.7, 127.6 (CH, Ph), 126.7 (C-2), 96.0 (C-1), 73.3, 71.0 (*C*H$_2$Ph), 75.3 (C-4), 69.9 (C-5), 69.6 (C-6), 68.4 (C-1′), 29.8, 29.7, 29.6, 29.5, 29.3, 26.1, 22.7 (C-2′ to C11′), 14.1 (C-12′) ppm. **HRMS**: Calcd. $[C_{32}H_{46}NaO_4]$ 517.3291, found 517.3290 (error –0.2 ppm).

Dodecyl 2,3-dideoxy-α-D-*erythro*-pyranoside (23). To a solution of compound **22a** (0.050g, 0.101 mmol) in MeOH (5 mL) and EtOAc (1 mL), was added a suspension of 10 % Pd/C (0.200g, wet) in MeOH (2 mL). Under N_2, triethylsilane was added dropwise (0.7 mL), leading to a visible evolution of H_2, and the solution was stirred overnight. After filtration of the catalyst through Celite, and evaporation of the solvent, title compound was obtained as a colorless oil in 51 % yield (16.3 mg). R_f (Petrol. ether/EtOAC, 1:1) = 0.5; $[\alpha]_D^{20}$ = +86° (*c*0.1, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 4.72 (d, $^3J_{1,2}$ = 3 Hz, 1 H, 1-H), 3.75 (dd, $^3J_{5,6a}$ = 2 Hz, $^3J_{6a,6b}$ = 11 Hz, 1 H, 6a-H), 3.67 (td, $^3J_{1'a,1'b}$ = 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1′a-H), 3.62 (dd, $^3J_{5,6b}$ = 5 Hz, 1 H, 6b-H), 3.47 (ddd, $^3J_{4,5}$ = 9 Hz, 1 H, H-5), 3.44–3.37 (m, 1 H, 4-H), 3.34 (td, 1 H, 1′b-H), 1.83–1.65 (m, 4 H, 2-H and 3-H), 1.60–1.51 (m, 2 H, 2′-H), 1.42–1.20 (m, 18 H, 3-H to 11′-H), 0.87 (t, $^3J_{11'12'}$ = 7 Hz, 3 H, H-12′) ppm. **^{13}C NMR** ($CDCl_3$) *δ* 95.3 (C-1), 73.3 (C-5), 66.0 (C-1′), 65.1 (C-4), 61.1 (C-6), 31.1, 28.8, 28.6, 28.5 (C-2′ to C-11′), 28.4, 21.8 (C3 and C2), 12.5 (C-12′) ppm. **HRMS**: Calcd. $[C_{18}H_{36}NaO_4]$ 339.2506, found 339.2503 (error 0.7 ppm).

Methyl 2,6-di-*O*-pivaloyl-α-D-glucopyranoside (24). To a solution of methyl α-D-glucopyranoside (2.02 g, 10.4 mmol) in pyridine (20 mL), a solution of pivaloyl chloride (2.2 equiv., 22.8 mmol, 2.8 mL) in DCM (4 mL) was added dropwise, at –78 °C. After stirring at –10 °C for 2h, the reaction was diluted with DCM (100 mL), washed with a 2M HCl solution until the odor of pyridine was no longer detected. The organic phase then washed with water, dried with $MgSO_4$, filtered and the solvents evaporated. The resulting residue was purified by CC eluted with petrol. ether/ EtOAc 5:1. Compound **24** was obtained as a white solid in 65 % (2.44 g) yield. Physical and spectroscopic data were in agreement with data reported in the literature.[13]

Methyl 2,6-di-*O*-pivaloyl-3,4-dideoxy-α-D-*erythro*-hexopyranoside (25) and methyl 4-deoxy-2,6-di-*O*-pivaloyl-α-D-*xylo*-hexopyranoside (26). Compound **24** (1 g, 2.75 mmol) was dissolved in DCM (30 mL) and pyridine (0.89 mL, 11.0 mmol, 4 equiv.), and cooled to –10 °C, under N_2. Trifluoromethanesulfonic anhydride (1.86 mL, 11.0 mmol, 4 equiv.) was then added dropwise to the stirring solution, which was then warmed to 2 °C and stirred for 2h30. The reaction was quenched by addition of 100 mL of cool distilled water, followed by extraction with DCM (2 × 100 mL). Organic phase was dried with $MgSO_4$, filtered and evaporated under reduced pressure, affording highly labile colorless syrup composed of methyl 2,6-di-*O*-pivaloyl-3,4-di-*O*-trifluoromethanesulfonyl-α-D-gluco-pyranoside. The syrup was dissolved in toluene (32 mL), tetra-*n*-butylammonium borohydride (4.180 g, 16.2 mmol, 5.9 equiv.) was added, and the reaction mixture was stirred at 85 °C overnight, cooled to room temperature and poured into ice cold water (100 mL). After extraction with DCM (2 × 50 mL), the organic phase was washed with saturated aqueous sodium hydrogen carbonate (2 × 50 mL) and water (50 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give a syrup that was purified by CC eluted with Hex/EtOAc, 10:1, to afford compound 27a as a colorless oil in 29 % yield (0.263 g) and compound 27b also as a colorless oil in 33 % yield (0.314 mg).

Methyl 2,6-di-*O*-pivaloyl-3,4-dideoxy-α-D-*erythro*-hexopyranoside (25). $[\alpha]_D^{20}$ = +82° (*c*1; $CHCl_3$); R_f (hex/EtOAc, 3:1)= 0.67; **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 4.78 (d, $^3J_{1,2}$ = 3 Hz, 1 H, 1-H), 4.72 (ddd, $^3J_{2,3ax}$ = 12 Hz, $^3J_{2,3eq}$ = 4 Hz, 1 H, 2-H), 4.11–4.00 (m, 2 H, 6-H), 3.97–3.89 (m, 1H, 5-H), 3.39 (s, 3 H, -OMe), 1.94 (qd, $^3J_{3ax,3eq}$ = 12 Hz, $^3J_{3ax,4eq}$ = $^3J_{3ax,4ax}$ = 4 Hz, 1 H, 3ax-H), 1.84–1.77 (m, 1 H, 3eq-H), 1.72 (ddd, $^3J_{4ax,4eq}$ = 13 Hz, 4eq-H), 1.53 (qd, 1 H, 4ax-H), 1.21 (s, 9 H, -OPiv), 1.19 (s, 9 H, -OPiv) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 178.3, 178.1 (C=O, Piv), 96.9 (C-1), 69.8 (C-2), 66.1 (C-5 and C-6), 55.0 (OMe), 38.8, 38.7 (Cq, -OPiv), 27.2, 27.0 (*C*H$_3$, -OPiv), 26.5 (C-4), 22.8 (C-3) ppm. **HRMS**: Calcd. $[C_{17}H_{30}NaO_6]$ 353.1935, found 353.1935 (error 0.0 ppm).

Methyl 4-deoxy-2,6-di-*O*-pivaloyl-α-D-*xylo*-hexopyranoside (26). R_f (hex/EtOAc, 3:1)= 0.58; $[\alpha]_D^{20}$ = +75° (*c*1; $CHCl_3$); R_f (hex/EtOAc, 3:1)= 0.58; **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 4.72 (d, $^3J_{1,2}$ = 4 Hz, 1 H, H-1), 4.55 (s, 1 H, OH), 4.30–4.22 (m, 2 H, 3-H and 5-H), 4.15–4.02 (m, 3 H, 6-H and 2-H), 3.43 (s, 3 H, -OMe), 2.02 (td, $^3J_{4e,5}$ = $^3J_{3,4e}$ = 3 Hz, $^3J_{4e,4a}$ = 14 Hz, 1 H, 4ax-H), 1.83 (ddd, $^3J_{4a,5}$ = $^3J_{3,4a}$ = 11 Hz, 1 H, 4ax-H), 1.21 (s, 9 H, -OPiv) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 178.2 (C=O, Piv), 101.0 (C-1), 68.2 (C-2), 67.9, 68.8 (C-5 and C-6), 61.3 (C-3), 55.9 (OMe), 38.8 (Cq, -OPiv), 34.0 (C-4), 27.2 (CH_3, -OPiv) ppm. **HRMS**: Calcd. [$C_{17}H_{30}NaO_7$] 369.1884, found 369.1883 (error 0.1 ppm).

Dodecyl 3,4-dideoxy-D-*erythro*-hexopyranosides (27a,b). Compound **25** (0.260 g, 0.787 mmol) and Amberlyst 15 (0.050 g) were suspended in dodecan-1-ol (2.41 mL, 10.75 mmol, 14 equiv.) and stirred at 95 °C for 20 h. Reaction was then cooled to r.t., diluted with DCM, the A-15 beads were filtered off and DCM was evaporated under reduced pressure. The residue was resuspended in 3 mL of MeOH:H_2O 50:50, and potassium hydroxide pellets (0.6 g) were added to the stirring solution. After 16 h at room temperature, reaction was diluted with MeOH (3 mL) and neutralized with IR-120. After filtration and evaporation of the solvent, the residue was purified by CC, eluted with hex/acetone, 4:1, affording the alfa anomer **27a** as a white solid in 36 % yield (0.0896 g), and the beta-anomer **27b** as a colorless oil, in 14 % yield (0.0338 g).

Dodecyl 3,4-dideoxy-α-D-*arabino*-hexopyranoside (27a). R_f (CyHex/EtOAc, 1:3) = 0.65; M.p. = 52.9.0–53.8 °C; $[\alpha]_D^{20}$ = +71° (*c*1, CH_2Cl_2); **^{1}H NMR** (400.13 MHz, $CDCl_3$, 25 °C): δ = 4.66 (d, $^3J_{1,2}$= 3 Hz, 1 H, H-1), 3.75–3.66 (m, 2 H, 5-H and 1′a-H), 3.55 (ddd, $^3J_{2,3ax}$ = 11 Hz, $^3J_{2,3eq}$ = 4 Hz, 1 H, 2-H), 3.46–3.37 (m, 2 H, 6-H and 1′b-H), 1.80 (qd, $^3J_{3ax,3eq}$ = 12 Hz, $^3J_{2,3eq}$ = 4 Hz, 1 H, 3eq-H), 1.75–1.68 (m, 1 H, 3ax-H), 1.67–1.54 (m, 3 H, 4eq-H and 2′-H), 1.45–1.34 (m, 3 H, 4ax-H, 3′-H), 1.33–1.21 (m, 16H, 4′-H to 11′-H), 0.87 (t, $^3J_{11',12'}$ = 7 Hz, 1 H, 12′-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = δ 99.8 (C-1), 70.1 (C-5), 69.6 (C-2), 68.8 (C-1′), 65.9 (C-6), 33.1, 30.8, 30.7, 30.5, 23.8 (C-2′, C-4′ to C-11′), 27.8, 27.4, 27.3 (C-3, C-4 and C-3′), 14.5 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{36}NaO_4$] 339.2506, found 339.2500 (error 1.6 ppm).

Dodecyl 3,4-dideoxy-β-D-*erythro*-hexopyranoside (27b). R_f (CyHex/EtOAc, 1:3)0.64; $[\alpha]_D^{20}$ = −22° (*c*0.2, CH_2Cl_2); **^{1}H NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 4.21 (d, $^3J_{1,2}$ = 8 Hz, 1 H, 1-H), 3.90 (td, $^3J_{1'a,1'b}$= 10 Hz, $^3J_{1'a,2'}$ = 7 Hz, 1 H, 1′a-H), 3.66–3.56 (m, 3 H, 5-H and 6-H), 3.51 (td, 1 H, 1′b-H), 3.43–3.35 (m, 1 H, 2-H), 2.14–2.08 (m, 1 H, 3ax-H), 1.97 (br s, 2 H, OH), 1.66–1.54 (m, 3 H, 2′-H and 4ax-H), 1.52–1.42 (m, 2, 3eq-H and 4eq-H), 1.35–1.15 (m, 18 H, 3′-H to 11′-H), 0.87 (t, $^3J_{11',12'}$ = 7 Hz, 3 H, 12′-H) ppm. **^{13}C NMR** (100.62 MHz, $CDCl_3$, 25 °C): δ = 105.3 (C-1), 76.4 (C-5), 69.9 (C-1′), 69.8 (C-2), 65.3 (C-6), 31.9, 29.7, 29.6, 29.4, 29.3, 28.9, 26.0, 25.9, 22.7 (C-3, C-4, and C-2′ to C11′), 14.1 (C-12′) ppm. **HRMS**: Calcd. [$C_{18}H_{36}NaO_4$] 339.2506, found 339.2507 (error −0.3 ppm).

Antimicrobial assays and bacterial strains. For results presented in Table 1, the broth microdilution method on Müller-Hinton medium was employed to determine the MIC values, according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.[14] Three strains of the *B. anthracis* (INSA private collection), *B. cereus* (ATCC 11778) and *E. faecalis* (ATCC 29212) were used. Compounds were incubated with bacteria for 16 h at 37 °C prior to determining the MIC, which is defined as the lowest concentration of the tested compounds at which no bacterial growth was observed.

Cytotoxicity. Caco-2 and HepG2 cell culture and viability assays were performed using a pre-established methodology.[15] Caco-2 and HepG2 cells were grown in DMEM high glucose supplemented with 10 % fetal bovine serum, glutamine (2 mM), penicillin (100 U/mL), and streptomycin (100 µg/mL), in a humidified incubator at 37 °C with a 5 % CO_2 atmosphere. The cells were trypsinized twice a week with trypsin/EDTA (0.05 %/0.02 %) and the medium was also changed twice a week. Determination of cell growth was performed using the MTT [3-(4,5-dimethylthiazol-2-*yl*)-2,5-diphenyltetrazolium bromide] assay. On day 1, 20,000 cells/well were seeded into 96-well plates in a volume of 100 µL. On day 2, the different drugs concentration (0.1–100 µM) were added to the plate. In all the experiments, the various drug-solvents (EtOH, DMSO) were added in each control to evaluate a possible solvent cytotoxicity. After the established incubation time with drugs,10 µL MTT (0.5 mg/mL) was added to each well, and after 3–4 h incubation at 37 °C, the supernatant was removed. The formazan crystals were solubilized using DMSO/EtOH (1:1) (100 µL) and the absorbance values at 570 nm and 630 nm were determined on the microplate reader Victor3 from Perkin Elmer Life Sciences.

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