Stereoselective Synthesis of the 3-Aminopropyl Glycosides of α-D-Xyl-(1→3)-β-D-Glc and α-D-Xyl-(1→3)-α-D-Xyl-(1→3)-β-D-Glc and of Their Corresponding *N*-Octanoyl Derivatives

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Abstract: The stereoselective synthesis of the spacer-armed disaccharide α-D-Xyl-(1→3)-β-D-Glc-*O*-$(CH_2)_3NH_2$ and trisaccharide α-D-Xyl-(1→3)-α-D-Xyl-(1→3)-β-D-Glc-*O*-$(CH_2)_3NH_2$, as well as of their *N*-octanoyl derivatives, was performed for their subsequent use as acceptors and reference samples in xylosyltransferase assays. These structures are found as O-linked glycans on epidermal growth factor (EGF) domains of several blood-clotting factors and Notch. The target products were prepared by glycosylation with a 3-O-acetylated xylosyl donor that was previously found to be an effective α-xylosylating agent. However, in this paper we show that the structure of the glycosyl acceptor could influence the stereochemical results of the glycosylation and even lead to reversed stereoselectivity in the case of one acceptor.

Key words: carbohydrates, glycosylations, stereoselectivity, α-xylosylations, remote participation

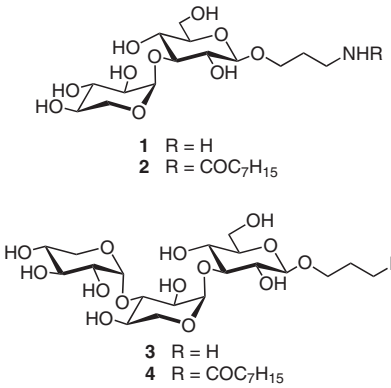

Figure 1 Oligosaccharide derivatives synthesized

In 1996, a novel enzyme able to transfer xylose to the disaccharide acceptor α-D-Xyl-(1→3)-β-D-Glc and, thus, form trisaccharide chain α-D-Xyl-(1→3)-α-D-Xyl-(1→3)-β-D-Glc was discovered in human cells.[1] Both the disaccharide and trisaccharide carbohydrate chains were found in bovine and human blood-clotting factors VII, IX, and protein Z.[2] Little is known about the functions of these oligosaccharides, but it was suggested that they may serve as regulators of coagulation activity.[3] Additionally, these O-linked glycans were linked to EGF repeats of the Notch receptor, where they might have a similar function as O-fucose-linked glycans.[4]

In this paper, we report the stereoselective synthesis of oligosaccharides **1** and **3** and their corresponding *N*-octanoyl derivatives **2** and **4** (Figure 1) for their further application as acceptor substrates and reference samples in xylosyltransferase assays. In addition to compounds **2** and **4**, other conjugates could be prepared from amines **1** and **3** and used as probes for biochemical investigations.

Previously reported syntheses of α-D-Xyl-(1→3)-β-D-Glc and α-D-Xyl-(1→3)-α-D-Xyl-(1→3)-β-D-Glc derivatives entailed the use of fully benzylated mono- and di-xylosyl donors.[5] In these cases, the glycosylation reaction proceeded with low stereoselectivity and gave a mixture of the corresponding α- and β-isomers that were difficult to separate.

We describe here the synthesis of oligosaccharide derivatives **1**–**4** using 3-*O*-acetyl-2,4-di-*O*-benzyl-D-xylopyranosyl 2,2,2-trichloroacetimidate (**5**). The acetyl group in this compound affords temporary protection of the hydroxy group at C-3, permitting further elongation of the appropriate oligosaccharide chain by 3-O-α-D-xylosylation. We have also used 3-O-acetylated donor **5** to explore the remote α-stereocontrolling effect of an *O*-acetyl group.[6–8] This effect arises from the anchimeric participation of the 3-*O*-acetyl group resulting in the formation of stabilized cation **II**. The nucleophilic attack of **II** is favored from the α-side, whereas attack of the nonstabilized cation **I** is possible from both the α- and β-sides (Scheme 1).

For the synthesis of trichloroacetimidate **5**, allyl α-D-xylopyranoside (**6**)[9] was first regioselectively transformed into the 2,4-di-O-benzylated derivative **7**;[5] then, 3-O-acetylation of **7** gave the fully protected allyl xylopyranoside **8** (Scheme 2). The presence of the *O*-acetyl group at C-3 was confirmed by the downfield shift of the H-3 signal in the ^{1}H NMR spectrum of **8** (δ = 5.50) compared with the data for nonacylated **7** (δ = 4.06). O-Deallylation[10] of **8** with palladium(II) chloride in methanol, followed by trichloroacetimidation[11] of the resulting hemiacetal using trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave xylosyl donor **5** as an

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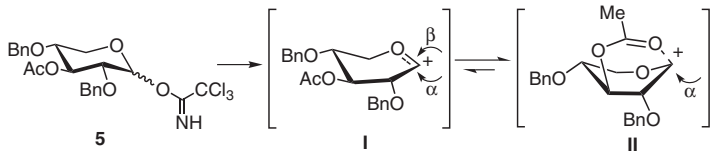
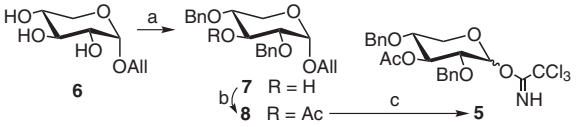


Scheme 1 Reactive sites of the nonstabilized **I** and stabilized glycosyl cations **II** formed from xylosyl donor **5**



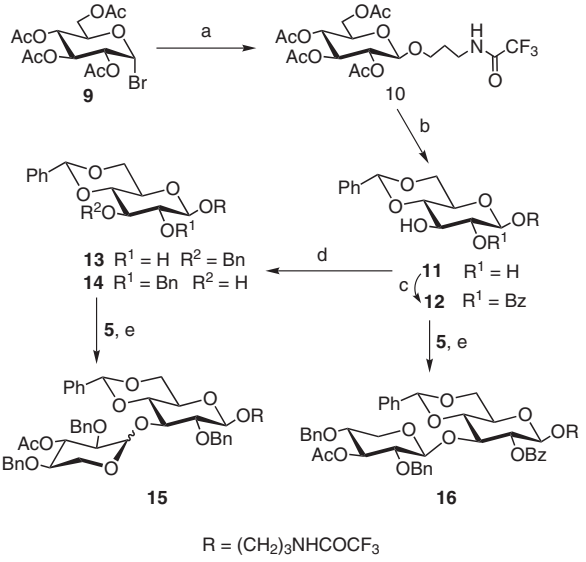
Scheme 2 *Reagents and conditions*: (a) 1. NaH (2 equiv), DMSO; 2. BnBr (2 equiv) (42% yield); (b) Ac_2O, py (99% yield); (c) 1. $PdCl_2$, MeOH; 2. CCl_3CN, DBU, CH_2Cl_2 (67% yield).

approximately 1:1 mixture (determined by NMR spectroscopy) of the α- and β-isomers in a total yield of 67%.

To assemble the α-D-Xyl-(1→3)-β-D-Glc disaccharide derivatives, the xylosylation of glucopyranosides **12** and **14** bearing a free hydroxy group at C-3 was studied first. To prepare acceptors **12** and **14**, *O*-acetyl-substituted glucopyranosyl bromide **9** was converted into β-glucopyranoside **10** by reaction with 3-(trifluoroacetamido)propanol in the presence of mercury(II) cyanide and mercury(II) bromide (Scheme 3). Deacetylation of **10** followed by 4,6-O-benzylidenation gave diol **11**. Regioselective benzoylation of diol **11** using benzoyl chloride via a stannylene acetal afforded the 2-O-benzoylated acceptor **12** in 74% yield. However, the dibutyltin oxide mediated benzylation of **11** using benzyl bromide in the presence of tetrabutylammonium bromide (TBAB) was less selective and gave the 2-*O*- and 3-*O*-benzyl-substituted monosaccharides **14** and **13** in 21 and 45% yields, respectively. The structures of these benzylated products were deduced from the ^{1}H NMR spectroscopic data of **13** and **14** and the corresponding acetylated derivatives.

The xylosylations of both acceptors **12** and **14** with donor **5** gave unexpected stereochemical results. Thus, the coupling of compounds **12** and **5** in dichloromethane at –40 °C promoted by trimethylsilyl trifluoromethanesulfonate (TMSOTf) resulted in the predominant formation of β-isomer **16** and not of the expected α-product, while the xylosylation of **14** produced a 1.4:1 mixture of the α- and β-isomers of **15**. The configurations of the glycosyl bonds formed in these products were deduced from the corresponding $J_{1',2'}$ coupling constants, which were 3.5 and 7.0 Hz for the α- and β-xylopyranosyl residues, respectively, in the mixture of **15** and 6.4 Hz for the β-xylopyranosyl unit in **16**. These exceptional stereochemical results from the xylosylations of spatially hindered bicyclic acceptors **12** and **14** could be connected with their structural organization, which does not permit coupling from the α-side. Such cases have been described previously.[12,13]

To overcome this limitation, 1,2:5,6-di-*O*-isopropylideneglucofuranose **17** was studied next as a xylosyl acceptor with better spatial availability of the hydroxy group at C-3 than in the benzylidene derivatives **12** and **14**. The results of the xylosylation reactions performed are presented in Table 1. Thus, xylosylation under the conditions used in the reaction with acceptors **12** and **14** afforded a mixture of the corresponding α-isomers ($J_{1',2'}$ = 3.4 Hz) and β-isomers ($J_{1',2'}$ = 8.2 Hz) in a ratio of 4.2:1 (entry 2). An increase in the reaction temperature to 20 °C (entry 1) reversed the stereoselectivity [(α/β) 1:1.4], while lowering it down to –90 °C (entry 3, reaction time of 15 min)



Scheme 3 *Reagents and conditions*: (a) $HO(CH_2)_3NHCOCF_3$, $Hg(CN)_2$, $HgBr_2$, CH_2Cl_2, r.t., 6 h (62% yield); (b) 1. NaOMe/MeOH, r.t.; 2. $PhCH(OMe)_2$, CSA, MeCN, 45 °C. (71% yield); (c) 1. Bu_2SnO, toluene, reflux; 2. BzCl, r.t., 1 h (74% yield); (d) 1. Bu_2SnO, toluene, reflux; 2. BnBr, TBAB, 60 °C, 5 h (45% yield of **13**, 21% yield of **14**); (e) TMSOTf, CH_2Cl_2, –40 °C, 50 min (65% yield of **15**, 72% yield of **16**)

Table 1 Study of the Stereoselectivity of the Coupling of **5** and **17**

Entry	Solvent	Promoter[a]	Temp (°C)	Ratio (α/β)	Total yield (%)
1	CH_2Cl_2	TMSOTf	20	1:1.4	72
2	CH_2Cl_2	TMSOTf	–40	4.2:1	87
3	CH_2Cl_2	TMSOTf	–90	9:1	86
4	CH_2Cl_2–Et_2O	TMSOTf	–40	2.5:1	61
5	CH_2Cl_2	$BF_3{\cdot}OEt_2$	–40	1:4	92

[a] 5 mol%.

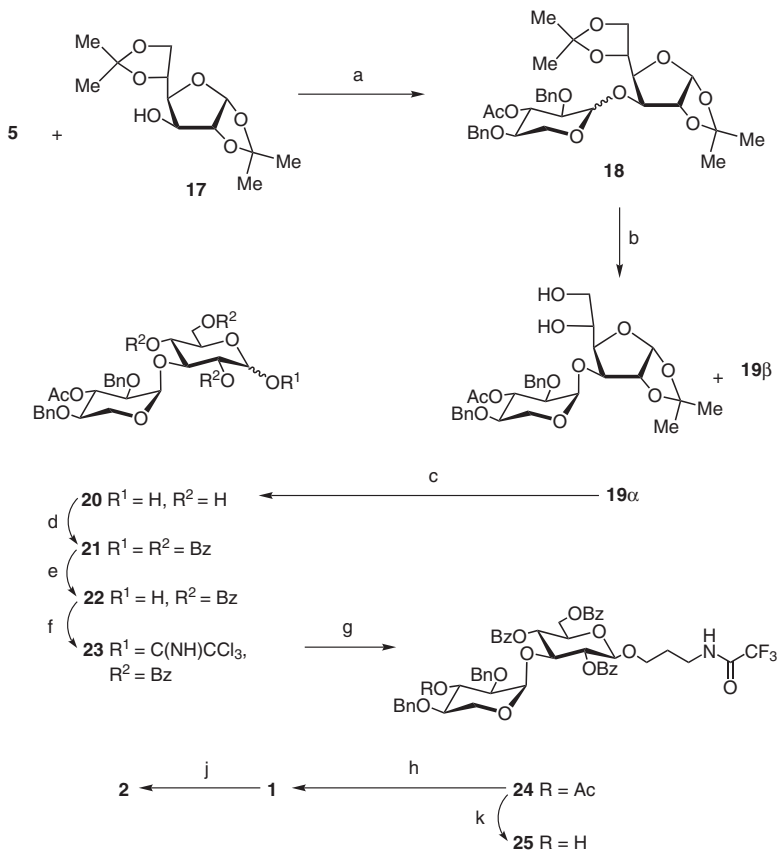
strongly favored the formation of the α-isomer [(α/β) 9:1] in good yield (86% total yield).

The coupling of compounds **5** and **17** in dichloromethane–diethyl ether (1:3) (entry 4) was less efficient than in dichloromethane (entry 2) and proceeded with lower stereoselectivity [(α/β) 2.5:1] and yield (61%), probably due to the solvation effect of diethyl ether. It is noteworthy that the boron trifluoride–diethyl ether complex promoted xylosylation (entry 5) gave the β-disaccharide as the major product [(α/β) 1:4].

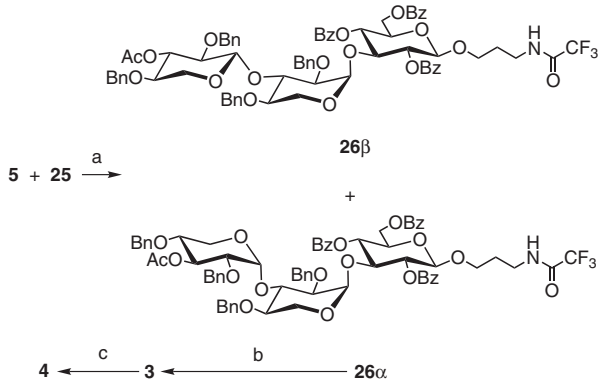
The protocol in entry 3 provided the highest α-stereoselectivity and, thus, was used for the preparation of the α-isomer of **18** (Scheme 4). The α- and β-isomers were separated by column chromatography after removal of the 5,6-acetonide under mild acid hydrolysis with aqueous acetic acid to give **19α** and **19β**.

Acid hydrolysis of **19α** with aqueous trifluoroacetic acid in ethyl acetate resulted in the removal of the 1,2-acetonide followed by the rearrangement of the furanose unit into the corresponding pyranose to give **20**. The presence of ethyl acetate prevented undesirable de-O-acetylation in the xylopyranose residue. Benzoylation of the resulting disaccharide **20** with benzoyl chloride in pyridine afforded the fully protected derivative **21**. Selective removal of the *O*-benzoyl group at C-1 in **21** was achieved in 72% yield using hydrazinium acetate in *N*,*N*-dimethylformamide.[14] Subsequent trichloroacetimidation of the product, **22**, afforded disaccharide donor **23**, which was coupled with 3-(trifluoroacetamido)propanol under catalysis using TMSOTf to give only the β-linked product **24** almost quantitatively. De-O-benzylation of **24** followed by saponification of the acyl group produced disaccharide **1** (as a salt with AcOH) in a yield of 62%. It was further reacted with an activated ester of octanoic acid[15] in the presence of triethylamine to give the target neoglycolipid **2** in 70% yield.

Selective acidic de-O-acetylation[8] of **24** gave disaccharide **25** in 79% yield (Scheme 4). The glycosylation of **25** with donor **5** at –40 °C produced a mixture of isomeric trisaccharides **26α** ($J_{1'',2''}$ = 3.3 Hz) and **26β** ($J_{1'',2''}$ = 7.9 Hz) with moderate stereoselectivity [(α/β) 2.7:1] and in a total yield of 70%. This reaction, performed at –90 °C, was more stereoselective [(α/β) 4.4:1] and efficient (Scheme 5), and the α- and β-isomers were separated by column chromatography to give **26α** and **26β** in 63% and 15% yields, respectively. The removal of all of the protecting groups in compound **26α** afforded the target trisaccharide **3** (as a salt with AcOH) in 66% yield. Compound **3** was then transformed into neoglycolipid **4** in 74% yield by N-octanoylation.



Scheme 4 *Reagents and conditions*: (a) see Table 1; (b) 80% aq AcOH, 45 °C (71% yield of **19α**, 8% yield of **19β**); (c) 90% aq TFA, EtOAc, 45 °C, 30 min (91% yield); (d) BzCl, py, 96 h (74% yield); (e) H_2NNH_2·AcOH, DMF, 4 °C, 18 h (72% yield); (f) CCl_3CN, DBU, CH_2Cl_2 (84% yield); (g) $HO(CH_2)_3NHCOCF_3$, TMSOTf, CH_2Cl_2, –40 °C, 5 min (98% yield); (h) 1. H_2, Pd/C, EtOAc; 2. 1.0 M aq NaOH, MeOH (62% yield); (j) *N*-(octanoyloxy)succinimide, Et_3N, DMF, r.t., 1 h (70% yield); (k) 0.5 M HCl in MeOH (79% yield).



Scheme 5 *Reagents and conditions*: (a) TMSOTf, CH_2Cl_2, –90 °C (63% yield of **26α**, 15% yield of **26β**); (b) 1. H_2, Pd/C, EtOAc; 2. 1.0 M aq NaOH, MeOH (66% yield); (c) *N*-(octanoyloxy)succinimide, Et_3N, DMF, r.t., 1 h (74% yield).

In conclusion, the synthesis of spacer-armed oligosaccharides **1** and **3** and their *N*-octanoyl derivatives **2** and **4** was achieved. The 3-O-acetylated xylosyl donor **5** was successfully applied to α-xylopyranosyl bond formations, but it was shown that the structure of the acceptor could influence the stereoselectivity of these glycosylations. The biological evaluation of the target oligosaccharides will be published elsewhere.

Thin-layer chromatography was performed on silica gel 60 F_{254} (Merck) with detection by charring with H_3PO_4. Liquid chromatography was performed on silica gel 60–200 μm (Fluka). Gel chromatography was performed on a BioBeads SX-3 (Bio Rad) column (2 × 70 cm) by elution with toluene at a flow rate of 1 mL/min, on a TSK HW-40(S) column (4 × 70 cm) by elution with 0.1 M aq AcOH at a flow rate of 0.8 mL/min, and on a Sephadex G-15 column (4 × 70 cm) by elution with H_2O at a flow rate of 1.5 mL/min. Optical rotations were determined with a Jasco DIP-360 digital polarimeter at 26–30 °C. All solvents used for the syntheses were purified according to conventional procedures.[16] ^{1}H NMR spectra for substituted compounds **5**–**26** were recorded on Bruker spectrometers WM-250, AM-300, and DRX-500 at 303 K. NMR spectra for oligosaccharides **1**–**4** were recorded in D_2O on a Bruker DRX-500 spectrometer with acetone as a reference (^{1}H NMR: 2.225 ppm). Gradient enhanced 2D gCOSY, gNOESY, and gHSQC experiments, as well as TOCSY experiments, were used for resonance assignment. Mass spectra of the compounds synthesized were recorded on a Finnigan LCQ mass spectrometer.

Allyl 2,4-Di-*O*-benzyl-3-*O*-acetyl-α-D-xylopyranoside (8)

To a solution of allyl xylopyranoside **7**[4] (2.00 g, 5.41 mmol) in py (8 mL) was added Ac_2O (1.5 mL). The mixture was kept for 5 h at r.t., after which MeOH (5 mL) was added dropwise while cooling. The mixture was stored for 20 min at r.t. and then diluted with toluene (20 mL) and concentrated in vacuo. Column chromatography of the residue gave xylopyranoside **8** as a colorless oil. Yield: 2.21 g (99%); $[\alpha]_D$ 81 (*c* 1, EtOAc); R_f = 0.32 (toluene–EtOAc, 20:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.02 (s, 3 H, CH_3), 3.42 (dd, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 9.9 Hz, 1 H, H-2), 3.53 (q, $J_{3,4} = J_{4,5a} = J_{4,5b}$ = 8.4 Hz, 1 H, H-4), 3.65 (m, 2 H, H-5), 3.97–4.20 (m, 2 H, CH_2=CHCH_2O), 4.58 (q, *J* = 12.1 Hz, 4 H, 2 CH_2Ph), 4.80 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1), 5.20–5.37 (m, 2 H, CH_2=CHCH$_2$O), 5.50 (t, $J_{2,3} = J_{3,4}$ = 10.0 Hz, 1 H, H-3), 5.95 (m, 1 H, CH_2=C*H*CH$_2$O), 7.15–7.40 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.89; H, 6.84. Found: C, 70.04; H, 6.96.

2,4-Di-*O*-benzyl-3-*O*-acetyl-D-xylopyranosyl 2,2,2-Trichloroacetimidate (5)

To a solution of allyl xylopyranoside **8** (2.15 g, 5.22 mmol) in anhyd MeOH (44 mL) was added $PdCl_2$ (461 mg, 2.61 mmol). The mixture was stirred for 2 h and then filtered through a Celite pad. The solution was neutralized with Et_3N (0.5 mL) and then concentrated. The residue was purified by flash chromatography (petroleum ether–EtOAc, 3:1) to give the hemiacetal as a white foam. A mixture of the resultant hemiacetal (1.51 g, 4.07 mmol), CCl_3CN (4 mL, 40.7 mmol), and DBU (100 μL) in anhyd CH_2Cl_2 (25 mL) was stirred for 1 h at –30 °C under Ar and then concentrated. The residue was purified by flash chromatography (silica gel passivated with Et_3N, petroleum ether–EtOAc, 7:1) to give the trichloroacetimidate **5** as a white solid. Yield: 1.81 g (67%); ratio (α/β) ~1:1 (determined by NMR spectroscopy); R_f = 0.68 (α), 0.56 (β) (toluene–EtOAc–Et_3N, 2:1:0.1).

α-Isomer

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3), 3.51–3.87 (m, 4 H, H-2, H-4, H-5), 4.50–4.70 (m, 4 H, 2 CH_2Ph), 5.53 (t, $J_{2,3} = J_{3,4}$ = 9.6 Hz, 1 H, H-3), 6.39 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1), 7.20–7.45 (m, 10 H, 2 Ph), 8.59 (s, 1 H, NH).

β-Isomer

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 3.51–3.70 (m, 3 H, H-2, H-4, H-5[a]), 4.03–4.19 (m, 3 H, CH_2Ph, H-5[b]), 4.50–4.70 (m, 2 H, CH_2Ph), 5.28 (t, $J_{2,3} = J_{3,4}$ = 7.8 Hz, 1 H, H-3), 5.92 (d, $J_{1,2}$ = 6.5 Hz, 1 H, H-1), 7.20–7.45 (m, 10 H, 2 Ph), 8.73 (s, 1 H, NH).

Anal. Calcd for $C_{23}H_{24}Cl_3NO_6$: C, 53.45; H, 4.68; N, 2.71. Found: C, 53.57; H, 4.72; N, 2.66.

3-(Trifluoroacetamido)propyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranoside (10)

To a solution of bromide **9** (4 g, 9.73 mmol) and 3-(trifluoroacetamido)propanol (1.47 g, 11.68 mmol) in anhyd CH_2Cl_2 (40 mL) were added $Hg(CN)_2$ (2.57 g, 10.22 mmol) and $HgBr_2$ (50 mg, 0.14 mmol). The mixture was stirred at r.t. for 6 h under Ar. Saturated solutions of aq KBr (120 mL) and aq $NaHCO_3$ (30 mL) were added to the mixture, which was then extracted with $CHCl_3$ (2 × 200 mL). The extracts were combined, dried (Na_2SO_4), and concentrated, and column chromatography of the residue gave glucopyranoside **10** as a white solid. Yield: 3.02 g (62%); $[\alpha]_D$ –15 (*c* 2, EtOAc); R_f = 0.52 (toluene–acetone, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70 (m, 2 H, CH_2CH_2CH$_2$), 2.00 (4 s, 12 H, 4 CH_3), 3.38 (2 m, 2 H, CH_2CH_2NH), 3.66 (m, 2 H, H-5, OC*H*H′CH$_2$), 3.85 (m, 1 H, OCH*H*′CH$_2$), 4.16 (m, 2 H, H-6), 4.48 (d, $J_{1,2}$ = 7.9 Hz, 1 H, H-1), 4.90 (t, $J_{1,2} = J_{2,3}$ = 8.1 Hz, 1 H, H-2), 5.01 (t, $J_{3,4} = J_{4,5}$ = 9.6 Hz, 1 H, H-4), 5.16 (t, $J_{2,3} = J_{3,4}$ = 9.4 Hz, 1 H, H-3), 7.15 (br s, 1 H, NH).

Anal. Calcd for $C_{19}H_{26}F_3NO_{11}$: C, 45.51; H, 5.23; N, 2.79. Found: C, 45.73; H, 4.99; N, 3.03.

3-(Trifluoroacetamido)propyl 4,6-*O*-Benzylidene-β-D-glucopyranoside (11)

To a stirred solution of **10** (2.5 g, 4.99 mmol) in anhyd MeOH (40 mL) was added 30% NaOMe in MeOH (0.2 mL, 0.55 mmol). The mixture was stirred for 4 h at r.t. and then was neutralized with Amberlite IR-120 (H^+). The resin was filtered off and the filtrate was concentrated. The residue was suspended in anhyd MeCN (40 mL) and then benzaldehyde dimethyl acetal (1.0 mL, 6.61 mmol) and (±)-CSA (0.1 g, 0.44 mmol) were added. The mixture was stirred for 3 h at 45 °C and then was neutralized with Et_3N, and the solvent was

evaporated in vacuo. The residue was purified by column chromatography (silica gel, toluene–EtOAc, 2:1) to give diol **11** as a white solid. Yield: 1.49 g (71%); $[\alpha]_D$ –31 (*c* 2, EtOAc); R_f = 0.57 (EtOAc).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.86 (m, 2 H, $CH_2CH_2CH_2$), 3.36–3.81 (m, 8 H, H-2, H-3, H-4, H-5, H-6^a, CH_2CH_2NH, $OCHH'CH_2$), 4.00 (m, 1 H, $OCHH'CH_2$), 4.29 (dd, $J_{5,6b}$ = 4.8 Hz, $J_{6a,6b}$ = 10.6 Hz, 1 H, H-6^b), 4.40 (d, $J_{1,2}$ = 7.7 Hz, 1 H, H-1), 5.50 (s, 1 H, PhC*H*), 7.25–7.40 (m, 5 H, Ph).

Anal. Calcd for $C_{18}H_{22}F_3NO_7$: C, 51.31; H, 5.26; N, 3.32. Found: C, 51.39; H, 5.51; N, 3.13.

3-(Trifluoroacetamido)propyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (12)

A mixture of diol **11** (500 mg, 1.19 mmol) and Bu_2SnO (311 mg, 1.25 mmol) in anhyd toluene (15 mL) was refluxed with azeotropic removal of H_2O to a volume of 4 mL. The mixture was then treated with BzCl (0.15 mL, 1.31 mmol), kept for 1 h at r.t., and then concentrated. Column chromatography (silica gel, toluene–EtOAc, 5:1) of the residue afforded the 2-*O*-benzoyl derivative **12** as a white solid. Yield: 463 mg (74%); $[\alpha]_D$ –32 (*c* 2, EtOAc); R_f = 0.37 (toluene–EtOAc, 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.73 (m, 2 H, $CH_2CH_2CH_2$), 2.67 (br s, 1 H, OH), 3.19–3.76 (m, 5 H, H-4, H-5, CH_2CH_2NH, $OCHH'CH_2$), 3.84 (t, $J_{6a,6b}$ = $J_{5,6a}$ = 10.2 Hz, 1 H, H-6^a), 3.96 (m, 1 H, $OCHH'CH_2$), 4.10 (t, $J_{2,3}$ = $J_{3,4}$ = 9.1 Hz, 1 H, H-3), 4.41 (dd, $J_{5,6b}$ = 4.9 Hz, $J_{6a,6b}$ = 10.5 Hz, 1 H, H-6^b), 4.70 (d, $J_{1,2}$ = 7.9 Hz, 1 H, H-1), 5.21 (t, $J_{1,2}$ = $J_{2,3}$ = 8.3 Hz, 1 H, H-2), 5.59 (s, 1 H, PhC*H*), 6.95 (br s, 1 H, NH), 7.12–8.15 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{25}H_{26}F_3NO_8$: C, 57.14; H, 4.99; N, 2.67. Found: C, 56.85; H, 5.21; N, 2.47.

3-(Trifluoroacetamido)propyl 3-*O*-Benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (13) and 3-(Trifluoroacetamido)propyl 2-*O*-Benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (14)

A mixture of diol **11** (300 mg, 0.71 mmol) and Bu_2SnO (197 mg, 0.79 mmol) in anhyd toluene (10 mL) was refluxed with azeotropic removal of H_2O to a volume of 2 mL. Then, BnBr (94 μL, 0.79 mmol) and TBAB (254 mg, 0.79 mmol) were added, and the mixture was kept for 5 h at 60 °C and then concentrated. Column chromatography (silica gel, toluene–EtOAc, 5:1) of the residue afforded the 2-*O*-benzyl derivative **14** as a white solid, as well as the 3-*O*-benzyl derivative **13**.

14

Yield: 76 mg (21%); $[\alpha]_D$ –20 (*c* 1, $CHCl_3$); R_f = 0.26 (toluene–EtOAc, 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.86 (m, 2 H, $CH_2CH_2CH_2$), 2.55 (br s, 1 H, OH), 3.31 (t, $J_{1,2}$ = $J_{2,3}$ = 8.5 Hz, 1 H, H-2), 3.37–3.55 (m, 4 H, H-4, H-5, CH_2CH_2NH), 3.70–3.78 (m, 2 H, H-6^a, $OCHH'CH_2$), 3.85 (dt, $J_{2,3}$ = $J_{3,4}$ = 8.7 Hz, $J_{3,OH}$ = 2.2 Hz, 1 H, H-3), 3.91 (m, 1 H, $OCHH'CH_2$), 4.31 (dd, $J_{5,6}$ = 4.9 Hz, $J_{6a,6b}$ = 10.4 Hz, 1 H, H-6^b), 4.49 (d, $J_{1,2}$ = 7.7 Hz, 1 H, H-1), 4.79, 4.83 (2 d, *J* = 11.6 Hz, 2 H, $PhCH_2$), 5.52 (s, 1 H, PhC*H*), 6.93 (br s, 1 H, NH), 7.25–7.48 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{25}H_{28}F_3NO_7$: C, 58.71; H, 5.52; N, 2.74. Found: C, 58.59; H, 5.78; N, 2.55.

13

Yield: 162 mg (45%); R_f = 0.37 (toluene–EtOAc, 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.87 (m, 2 H, $CH_2CH_2CH_2$), 2.55 (br s, 1 H, OH), 3.38–3.58 (m, 3 H, H-2, H-5, $CH_2CHH'NH$), 3.59–3.74 (m, 4 H, H-3, H-4, $CH_2CHH'NH$, $OCHH'CH_2$), 3.77 (t, $J_{5,6a}$ = $J_{6a,6b}$ = 10.3 Hz, 1 H, H-6^a), 4.04 (m, 1 H, $OCHH'CH_2$), 4.33 (dd, $J_{5,6b}$ = 4.9 Hz, $J_{6a,6b}$ = 10.5 Hz, 1 H, H-6^b), 4.41 (d, $J_{1,2}$ = 7.8 Hz, 1 H, H-1), 4.73, 4.98 (2 d, *J* = 11.8 Hz, 2 H, $PhCH_2$), 5.55 (s, 1 H, PhC*H*), 7.25–7.48 (m, 11 H, 2 Ph, NH).

To confirm the structures of **13** and **14**, small portions (~4–5 mg) of the compounds were acetylated as described for preparation **8**.

Acetylated derivative of **13**

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.85 (m, 2 H, $CH_2CH_2CH_2$), 1.99 (s, 3 H, CH_3), 3.30–3.62 (m, 5 H, H-3, H-4, H-5, CH_2CH_2NH), 3.72–3.81 (m, 2 H, H-6^a, $OCHH'CH_2$), 3.95 (m, 1 H, $OCHH'CH_2$), 4.33 (dd, $J_{5,6b}$ = 4.7 Hz, $J_{6a,6b}$ = 10.2 Hz, 1 H, H-6^b), 4.40 (d, $J_{1,2}$ = 7.9 Hz, 1 H, H-1), 4.73 (q, *J* = 12.1 Hz, 2 H, $PhCH_2$), 4.93 (t, $J_{1,2}$ = $J_{2,3}$ = 8.2 Hz, 1 H, H-2), 5.48 (s, 1 H, PhC*H*), 6.95 (br s, 1 H, NH), 7.08–7.53 (m, 10 H, 2 Ph).

Acetylated derivative of **14**

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.88 (m, 2 H, $CH_2CH_2CH_2$), 1.96 (s, 3 H, CH_3), 3.38 (t, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9.1 Hz, 1 H, H-2), 3.42–3.57 (m, 4 H, H-4, H-5, CH_2CH_2NH), 3.72 (t, $J_{5,6a}$ = $J_{6a,6b}$ = 10.3 Hz, 1 H, H-6^a), 3.79 (m, 1 H, $OCHH'CH_2$), 3.93 (m, 1 H, $OCHH'CH_2$), 4.32 (dd, $J_{5,6b}$ = 4.8 Hz, $J_{6a,6b}$ = 10.4 Hz, 1 H, H-6^b), 4.56 (d, $J_{1,2}$ = 7.7 Hz, 1 H, H-1), 4.63, 4.78 (2 d, *J* = 11.4 Hz, 2 H, $PhCH_2$), 5.31 (t, $J_{2,3}$ = $J_{3,4}$ = 9.4 Hz, 1 H, H-3), 5.46 (s, 1 H, PhC*H*), 6.90 (br s, 1 H, NH), 7.05–7.48 (m, 10 H, 2 Ph).

Glycosylation; General Procedure

To a solution of the glycosyl donor (1.1 mmol) and glycosyl acceptor (1.0 mmol) in anhyd CH_2Cl_2 (5 mL) under Ar was added 1 M TMSOTf in CH_2Cl_2 (50 μL) at –40 °C, and the mixture was stirred. The mixture was neutralized with Et_3N and evaporated. Column chromatography of the residue (silica gel, toluene–EtOAc, 15:1 to 7:1), followed by chromatography on a BioBeads SX-3 gel column gave the glycosylation product.

3-(Trifluoroacetamido)propyl 3-*O*-Acetyl-2,4-di-*O*-benzyl-D-xylopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (15)

Glycosylation of monosaccharide **14** (60 mg, 0.117 mmol) with trichloroacetimidate **5** (63 mg, 0.126 mmol) as described in the general procedure was complete within 50 min and gave disaccharide **15**. Yield: 66 mg (65%); R_f = 0.42 (toluene–EtOAc, 3:1).

α-Isomer

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.86 (m, 2 H, $CH_2CH_2CH_2$), 2.00 (s, 3 H, CH_3), 3.23 (dd, $J_{1',2'}$ = 3.5 Hz, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 3.36–3.52 (m, 7 H, H-2, H-5, H-4′, H-5′, CH_2CH_2NH), 3.72 (t, $J_{5,6a}$ = $J_{6a,6b}$ = 10.3 Hz, 1 H, H-6^a), 3.75–3.94 (m, 3 H, H-4, OCH_2CH_2), 4.03 (t, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, 1 H, H-3), 4.17 (d, *J* = 12.8 Hz, 1 H, $PhCHH'$), 4.33 (dd, $J_{5,6b}$ = 5.0 Hz, $J_{6a,6b}$ = 10.5 Hz, 1 H, H-6^b), 4.38–4.55 (m, 4 H, H-1, $PhCH_2$, $PhCHH'$), 4.82 (s, 2 H, $PhCH_2$), 5.38 (s, 1 H, PhC*H*), 5.46 (m, 2 H, H-1′, H-3′), 6.85–7.39 (m, 20 H, 4 Ph).

β-Isomer

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.85 (m, 2 H, $CH_2CH_2CH_2$), 1.95 (s, 3 H, CH_3), 3.11 (t, $J_{5a',5b'}$ = $J_{4',5a'}$ = 9.6 Hz, 1 H, H-5$^{a'}$), 3.35 (t, $J_{1',2'}$ = $J_{2',3'}$ = 8.8 Hz, 1 H, H-2′), 3.40–3.56 (m, 5 H, H-2, H-5, H-4′, CH_2CH_2NH), 3.63 (t, $J_{3,4}$ = $J_{4,5}$ = 9.3 Hz, 1 H, H-4), 3.77 (m, 2 H, H-6^a, $OCHH'CH_2$), 3.90 (m, 2 H, H-5$^{b'}$, $OCHH'CH_2$), 4.06 (t, $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz, 1 H, H-3), 4.13 (q, *J* = 12.3 Hz, 2 H, $PhCH_2$), 4.35 (dd, $J_{5,6b}$ = 4.8 Hz, $J_{6a,6b}$ = 10.3 Hz, 1 H, H-6^b), 4.50 (d, $J_{1,2}$ = 5.3 Hz, 1 H, H-1), 4.57–4.88 (m, 4 H, 2 $PhCH_2$), 4.92 (d, $J_{1',2'}$ = 7.0 Hz, 1 H, H-1′), 5.14 (t, $J_{2',3'}$ = $J_{3',4'}$ = 8.9 Hz, 1 H, H-3′), 5.55 (s, 1 H, PhC*H*), 6.92 (br s, 1 H, NH), 7.12–7.55 (m, 20 H, 4 Ph).

3-(Trifluoroacetamido)propyl 3-*O*-Acetyl-2,4-di-*O*-benzyl-β-D-xylopyranosyl-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (16)

Glycosylation of monosaccharide **12** (60 mg, 0.114 mmol) with trichloroacetimidate **5** (63 mg, 0.126 mmol) as described in the general procedure was complete within 50 min and gave disaccharide **16**. Yield: 72 mg (72%); R_f = 0.47 (toluene–EtOAc, 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.70 (m, 5 H, CH_3, $CH_2CH_2CH_2$), 3.12 (dd, $J_{4',5a'}$ = 8.6 Hz, $J_{5a',5b'}$ = 11.8 Hz, 1 H, H-5$^{a'}$), 3.22 (m, 2 H, H-2′, $CH_2CHH'NH$), 3.40–4.00 (m, 8 H, H-4, H-5, H-6^a, H-4′, H-5$^{b'}$, $CH_2CHH'NH$, OCH_2CH_2), 4.23–4.33 (m, 6 H, H-3, H-6^b, 2 PhCH_2), 4.65 (d, $J_{1,2}$ = 7.9 Hz, 1 H, H-1), 4.71 (d, $J_{1',2'}$ = 6.4 Hz, 1 H, H-1′), 4.97 (t, $J_{2',3'}$ = $J_{3',4'}$ = 8.5 Hz, 1 H, H-3′), 5.37 (t, $J_{1,2}$ = $J_{2,3}$ = 8.4 Hz, 1 H, H-2), 5.58 (s, 1 H, PhC*H*), 6.92–7.95 (m, 20 H, 4 Ph).

3-*O*-Acetyl-2,4-di-*O*-benzyl-D-xylopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (18)

Glycosylation of monosaccharide **17** (619 mg, 2.38 mmol) with trichloroacetimidate **5** (1.35 g, 2.62 mmol) as described in the general procedure, but at –90 °C, gave the product **18** within 15 min as a white foam. Yield: 1.26 g (86%); ratio (α/β) isomers ~9:1 (determined by NMR spectroscopy); R_f = 0.67 (toluene–EtOAc, 3:1).

α-Isomer

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21, 1.33, 1.41, 1.50, 2.05 (5 s, 15 H, 5 CH_3), 3.41 (dd, $J_{1',2'}$ = 3.4 Hz, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 3.54 (m, 1 H, H-4′), 3.57–3.80 (m, 2 H, H-5′), 3.95–4.50 (m, 5 H, H-3, H-4, H-5, H-6), 4.50–4.75 (m, 5 H, H-2, 2 CH_2Ph), 5.21 (d, $J_{1',2'}$ = 3.4 Hz, 1 H, H-1′), 5.39 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.5 Hz, 1 H, H-3′), 5.93 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1), 7.20–7.40 (m, 10 H, 2 Ph).

β-Isomer

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25, 1.35, 1.45, 1.50, 1.95 (5 s, 15 H, 5 CH_3), 3.23 (t, $J_{1',2'}$ = $J_{2',3'}$ = 8.2 Hz, 1 H, H-2′), 3.29 (m, 1 H, H-5$^{a'}$), 3.52 (m, 1 H, H-4′), 4.00 (dd, $J_{4',5b'}$ = 5.3 Hz, $J_{5a',5b'}$ = 12.1 Hz, 1 H, H-5$^{b'}$), 4.03–4.60 (m, 9 H, CH_2Ph, H-2, H-3, H-4, H-5, H-6, H-1′), 4.67 (q, J = 11.4 Hz, 2 H, CH_2Ph), 5.14 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.2 Hz, 1 H, H-3′), 5.77 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 7.20–7.40 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{33}H_{42}O_{11}$: C, 64.48; H, 6.89. Found: C, 64.21; H, 6.74.

3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-1,2-*O*-isopropylidene-α-D-glucofuranose (19α)

A solution of disaccharide product **18** (1.21 g, 1.97 mmol) in 80% aq AcOH (40 mL) was kept for 4 h at 45 °C, and then the mixture was concentrated. Column chromatography of the residue (petroleum ether–EtOAc, 2:3) gave the individual disaccharide **19α**. Yield: 803 mg (71%); $[\alpha]_D$ 68 (*c* 1, EtOAc); R_f = 0.32 (petroleum ether–EtOAc, 2:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27, 1.49, 2.04 (3 s, 9 H, 3 CH_3), 3.46 (dd, $J_{1',2'}$ = 3.5 Hz, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 3.50–4.25 (m, 8 H, H-3, H-4, H-5, H-6, H-4′, H-5a′, H-5b′), 4.49–4.74 (m, 5 H, H-1′, 2 CH_2Ph), 4.78 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-2), 5.41 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.6 Hz, 1 H, H-3′), 5.92 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1), 7.25–7.40 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{30}H_{38}O_{11}$: C, 62.71; H, 6.67. Found: C, 62.39; H, 6.81.

In addition, isomeric **19β** was isolated from the mixture. Yield: 95 mg (8%); R_f = 0.26 (petroleum ether–EtOAc, 2:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26, 1.40, 2.00 (3 s, 9 H, 3 CH_3), 3.29 (t, $J_{1',2'}$ = $J_{2',3'}$ = 7.4 Hz, 1 H, H-2′), 3.35 (m, 1 H, H-5$^{a'}$), 3.50 (m, 1 H, H-4′), 4.06 (m, 1 H, H-5$^{b'}$), 4.12–4.68 (m, 11 H, 2 CH_2Ph, H-2, H-3, H-4, H-5, H-6, H-1′), 5.15 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.6 Hz, 1 H, H-3′), 5.81 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 7.17–7.42 (m, 10 H, 2 Ph).

3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-D-glucopyranose (20)

To a solution of disaccharide **19α** (225 mg, 0.39 mmol) in EtOAc (7 mL) was added 90% aq TFA (7 mL). The mixture was kept for 30 min at 45 °C and then was concentrated. Column chromatography of the residue ($CHCl_3$–MeOH, 15:1 to 10:1) gave product **20** as a colorless oil. Yield: 191 mg (91%); ratio (α/β) ~1:1 (determined by NMR spectroscopy); R_f = 0.20 ($CHCl_3$–MeOH, 10:1).

α-Isomer

^{1}H NMR (250 MHz, CD_3OD): δ = 1.95 (s, 3 H, CH_3), 3.43–4.12 (m, 10 H, H-2, H-3, H-4, H-5, H-6, H-2′, H-4′, H-5′), 4.50–4.81 (m, 4 H, 2 CH_2Ph), 5.11 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.36 (t, $J_{2,3}$ = $J_{3,4}$ = 9.6 Hz, 1 H, H-3′), 5.53 (d, $J_{1',2'}$ = 2.0 Hz, 1 H, H-1′), 7.25–7.40 (m, 10 H, 2 Ph).

β-Isomer

^{1}H NMR (250 MHz, CD_3OD): δ = 1.95 (s, 3 H, CH_3), 3.25–4.12 (m, 10 H, H-2, H-3, H-4, H-5, H-6, H-2′, H-4′, H-5′), 4.50–4.81 (m, 5 H, 2 CH_2Ph, H-1), 5.34 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.6 Hz, 1 H, H-3′), 5.53 (d, $J_{1',2'}$ = 2.0 Hz, 1 H, H-1′), 7.25–7.40 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{27}H_{34}O_{11}$: C, 60.67; H, 6.41. Found: C, 60.42; H, 6.72.

Benzoyl 3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-glucopyranoside (21)

A solution of disaccharide **20** (200 mg, 0.37 mmol) and BzCl (1 mL, 10.90 mmol) in py (5 mL) was stirred for 96 h at r.t. Then, H_2O (40 mL) was added and the suspension formed was extracted with CH_2Cl_2 (3 × 20 mL). The extracts were combined, dried ($MgSO_4$), and concentrated. Column chromatography of the residue (silica gel, toluene–EtOAc, 20:1) gave product **21** as a white solid. Yield: 260 mg (74%); ratio (α/β) ~1:1 (determined by NMR spectroscopy); R_f = 0.59 (toluene–EtOAc, 7:1).

α-Isomer

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, CH_3), 3.09–3.43 (m, 4 H, H-2′, H-4′, H-5′), 3.58–4.70 (m, 8 H, 2 CH_2Ph, 3-H, 5-H, 6-H), 4.92 (d, $J_{1',2'}$ = 3.2 Hz, 1 H, H-1′), 5.26 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.5 Hz, 1 H, H-3′), 5.59 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 9.8 Hz, 1 H, H-2), 5.80 (t, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, 1 H, H-4), 6.76 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1), 6.90–8.15 (m, 30 H, 6 Ph).

β-Isomer

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, CH_3), 3.09–3.43 (m, 4 H, H-2′, H-4′, H-5′), 3.58–4.70 (m, 8 H, 2 CH_2Ph, 3-H, 5-H, 6-H), 4.96 (d, $J_{1',2'}$ = 3.3 Hz, 1 H, H-1′), 5.35 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.7 Hz, 1 H, H-3′), 5.64–5.77 (m, 2 H, H-2, H-4), 6.23 (d, $J_{1,2}$ = 6.9 Hz, 1 H, H-1), 6.90–8.15 (m, 30 H, 6 Ph).

Anal. Calcd for $C_{55}H_{50}O_{15}$: C, 69.46; H, 5.30. Found: C, 69.61; H, 5.38.

3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-glucopyranose (22)

To a solution of disaccharide **21** (240 mg, 0.25 mmol) in anhyd DMF (10 mL) was added H_2NNH_2·AcOH (440 mg, 4.8 mmol). The mixture was stirred for 18 h at 4 °C, then brine (50 mL) was added and the mixture was extracted with EtOAc (3 × 60 mL). The extracts were combined, dried ($MgSO_4$), concentrated. Column chromatography of the residue (silica gel, toluene–EtOAc, 8:1) gave disaccharide **22** as a white solid. Yield: 152 mg (72%); ratio (α/β) ~10:1 (NMR); R_f = 0.33 (toluene–EtOAc, 5:1).

α-Isomer

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.60 (s, 3 H, CH_3), 3.13 (dd, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 3.18–3.73 (m, 3 H, H-4′, H-5′), 3.79–4.68 (m, 8 H, H-3, H-5, H-6, 2 CH_2Ph), 5.02 (d, $J_{1',2'}$ = 3.5 Hz, 1 H, H-1′), 5.26 (m, 2 H, H-2, H-3′), 5.64 (d, $J_{1,2}$ = 3.4 Hz, 1 H, H-1), 5.70 (t, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, 1 H, H-4), 6.85–8.15 (m, 25 H, 5 Ph).

β-Isomer

Selected ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.88 (d, $J_{1,2}$ = 7.4 Hz, 1 H, H-1), 5.37 (t, $J_{2',3'}$ = $J_{3',4'}$ = 8.2 Hz, 1 H, H-3′).

Anal. Calcd for $C_{48}H_{46}O_{14}$: C, 68.08; H, 5.47. Found: C, 68.31; H, 5.65.

3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-D-glucopyranosyl Trichloroacetimidate (23)

A mixture of hemiacetal **22** (250 mg, 0.30 mmol), CCl_3CN (0.3 mL, 3 mmol), and DBU (20 μL) in anhyd CH_2Cl_2 (4 mL) was stirred for 1 h at –30 °C under Ar and then was concentrated. The residue was purified by flash chromatography (silica gel passivated with Et_3N, petroleum ether–EtOAc, 5:1) to give the trichloroacetimidate **23** as a white foam. Yield: 250 mg (84%); ratio (α/β) ~25:1 (determined by NMR spectroscopy); R_f = 0.50 (toluene–EtOAc–Et_3N, 5:1:0.1).

α-Isomer

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.77 (s, 3 H, CH_3), 3.10 (dd, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 3.18–3.30 (m, 2 H, H-4′, H-5$^{a'}$), 3.62 (t, $J_{4',5b'}$ = $J_{5a',5b'}$ = 10.9 Hz, 1 H, H-5$^{b'}$), 3.77–4.27 (m, 4 H, 2 CH_2Ph), 4.37 (dd, $J_{5,6a}$ = 5.3 Hz, $J_{6a,6b}$ = 12.3 Hz, 1 H, H-6^a), 4.47–4.63 (m, 3 H, H-3, H-5, H-6^b), 4.90 (d, $J_{1',2'}$ = 3.6 Hz, 1 H, H-1′), 5.22 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.6 Hz, 1 H, H-3′), 5.51 (dd, $J_{1,2}$ = 3.9 Hz, $J_{2,3}$ = 9.6 Hz, 1 H, H-2), 5.74 (t, $J_{3,4}$ = $J_{4,5}$ = 9.9 Hz, 1 H, H-4), 6.70 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 6.87–8.05 (m, 25 H, 5 Ph), 8.57 (s, 1 H, NH).

β-Isomer

Selected ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.18 (d, $J_{1,2}$ = 6.0 Hz, 1 H, 1-H), 8.63 (s, 1 H, NH).

Anal. Calcd for $C_{50}H_{46}Cl_3NO_{14}$: C, 60.58; H, 4.68; N, 1.41. Found: C, 60.72; H, 4.94; N, 1.39.

3-(Trifluoroacetamido)propyl 3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (24)

Glycosylation of 3-(trifluoroacetamido)propanol (82 mg, 0.48 mmol) with trichloroacetimidate **23** (236 mg, 0.24 mmol; twofold excess) as described in the general procedure was complete within 5 min and gave disaccharide **24** as a white solid. Yield: 235 mg (98%); $[\alpha]_D$ 29 (*c* 1, EtOAc); R_f = 0.39 (toluene–EtOAc, 5:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.85 (m, 5 H, CH_3, $CH_2CH_2CH_2$), 3.18 (dd, $J_{1',2'}$ = 3.5 Hz, $J_{2',3'}$ = 10.0 Hz, 1 H, H-2′), 3.23–3.68 (m, 6 H, OCH_2CH_2, CHN, H-4′, H-5′), 3.94–4.31 (m, 7 H, 2 CH_2Ph, H-3, H-5, CHN), 4.48 (dd, $J_{5,6a}$ = 5.7 Hz, $J_{6a,6b}$ = 11.9 Hz, 1 H, H-6^a), 4.70 (dd, $J_{5,6b}$ = 4.0 Hz, $J_{6a,6b}$ = 11.9 Hz, 1 H, H-6^b), 4.80 (d, $J_{1,2}$ = 6.0 Hz, 1 H, H-1), 4.93 (d, $J_{1',2'}$ = 3.5 Hz, 1 H, H-1′), 5.26–5.32 (m, 2 H, H-2, H-3′), 5.54 (t, $J_{3,4}$ = $J_{4,5}$ = 7.6 Hz, 1 H, H-4), 6.95–8.00 (m, 25 H, 5 Ph).

Anal. Calcd for $C_{53}H_{52}F_3NO_{15}$: C, 63.66; H, 5.24; N, 1.40. Found: C, 63.65; H, 5.40; N, 1.39.

3-Aminopropyl α-D-Xylopyranosyl-(1→3)-β-D-glucopyranoside (1)

To a solution of disaccharide **24** (120 mg, 0.12 mmol) in MeOH (3 mL) and EtOAc (2 mL) was added 10% Pd/C (10 mg). The mixture was degassed, and the flask was filled with H_2. The mixture was stirred for 4 h, filtered through a Celite pad, and concentrated in vacuo. The residue was purified by flash chromatography (toluene–EtOAc, 1:1) to give the diol as a white solid. This compound was dissolved in MeOH (0.8 mL), 1.0 M aq NaOH (0.8 mL) was added, and the mixture was kept for 24 h at r.t. Then, the mixture was neutralized with 10% aq AcOH and concentrated. The deprotected disaccharide **1** was isolated as a salt with AcOH by chromatography on a TSK HW-40(S) gel column. Yield: 32 mg (0.075 mmol, 62%); $[\alpha]_D$ 63 (*c* 1, H_2O).

^{1}H NMR (500 MHz, D_2O): δ = 1.88 (s, 3 H, CH_3), 1.99 (m, 2 H, $CH_2CH_2CH_2$), 3.14 (t, *J* = 7.0 Hz, 2 H, CH_2CH_2NH), 3.36 (t, $J_{1,2}$ = $J_{2,3}$ = 8.2 Hz, 1 H, H-2), 3.45 (m, 1 H, H-5), 3.52 (dd, $J_{1',2'}$ = 3.8 Hz, $J_{2',3'}$ = 9.5 Hz, 1 H, H-2′), 3.56–3.72 (6 H, m, H-3, H-4, H-6^a, H-3′, H-4′, H-5$^{a'}$), 3.77–3.91 (m, 3 H, H-6^b, H-5$^{b'}$, OC*H*′CH_2), 4.03 (m, 1 H, OC*H*′CH_2), 4.47 (d, $J_{1,2}$ = 8.1 Hz, 1 H, H-1), 5.29 (d, $J_{1',2'}$ = 3.7 Hz, 1 H, H-1′).

^{13}C NMR (125 MHz, D_2O): δ = 24.46 ($CH_2CH_2CH_2$), 38.75 (CH_2CH_2NH), 61.69 (C-6), 62.67 (C-5′), 69.00 (OCH_2CH_2), 70.50 (C-4′), 71.30 (C-4), 72.75, 72.87 (C-2, C-2′), 74.17 (C-3′), 76.84 (C-5), 82.97 (C-3), 100.25 (C-1′), 103.52 (C-1).

MS (MALDI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{28}NO_{10}$: 370.171; found: 370.171.

3-(Trifluoroacetamido)propyl 2,4-Di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (25)

To a solution of compound **24** (190 mg, 0.19 mmol) in anhyd CH_2Cl_2 (1 mL) was added a solution of HCl in MeOH (0.5 M), prepared by treating anhyd MeOH (5 mL) with AcCl (0.2 mL). The mixture was kept for 8 h at r.t., then H_2O (40 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 40 mL). The extracts were combined, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (silica gel, toluene–EtOAc, 7:1) to give disaccharide **25** as a white solid. Yield: 144 mg (79%); $[\alpha]_D$ 24 (*c* 1, EtOAc); R_f = 0.34 (toluene–EtOAc, 5:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (m, 2 H, $CH_2CH_2CH_2$), 3.02 (dd, $J_{1',2'}$ = 3.4 Hz, $J_{2',3'}$ = 9.5 Hz, 1 H, H-2′), 3.13–3.29 (m, 3 H, H-4′, H-5$^{a'}$, CH_2CH*H*′NH), 3.38–3.57 (m, 2 H, H-5$^{b'}$, CH_2CH*H*′NH), 3.62 (m, 1 H, OC*H*H′CH_2), 3.85 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.3 Hz, 1 H, H-3′), 3.89–4.08 (m, 3 H, H-5, PhC*H*H′O, OCH*H*′CH_2), 4.22–4.46 (m, 5 H, H-3, H-6^a, PhCH*H*′O, PhCH_2), 4.69 (m, 2 H, H-1, H-6^b), 4.84 (d, $J_{1',2'}$ = 3.4 Hz, 1 H, H-1′), 5.32 (t, $J_{1,2}$ = $J_{2,3}$ = 8.2 Hz, 1 H, H-2), 5.62 (t, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, 1 H, H-4), 6.95–8.05 (m, 25 H, 5 Ph).

Anal. Calcd for $C_{51}H_{50}F_3NO_{14}$: C, 63.94; H, 5.26; N, 1.46. Found: C, 63.72; H, 5.45; N, 1.50.

3-(Trifluoroacetamido)propyl 3-*O*-Acetyl-2,4-di-*O*-benzyl-α-D-xylopyranosyl-(1→3)-2,4-*O*-di-benzyl-α-D-xylopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-glucopyranoside (26α)

Glycosylation of disaccharide **25** (140 mg, 0.15 mmol) with trichloroacetimidate **5** (93 mg, 0.18 mmol) as described in the general procedure, but at –90 °C, gave trisaccharide **26α** as a white foam. Yield: 126 mg (63%); $[\alpha]_D$ 24 (*c* 1, EtOAc); R_f = 0.34 (toluene–EtOAc, 5:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.73 (m, 2 H, $CH_2CH_2CH_2$), 1.94 (s, 3 H, CH_3), 3.18–3.27 (m, 3 H, H-2′, H-2″, CH_2CH*H*′NH), 3.32–3.64 (m, 7 H, H-4′, H-4″, H-5′, H-5$^{a''}$, CH_2CH*H*′NH, OC*H*H′CH_2), 3.82 (t, $J_{4'',5b''}$ = $J_{5a'',5b''}$ = 11.1 Hz, 1 H, H-5$^{b''}$), 3.94 (m, 1 H, OCH*H*′CH_2), 4.05–4.49 (m, 12 H, 4 PhCH_2, H-3, H-5, H-3′, H-6^a), 4.72 (m, 3 H, 1-H, 1-H′, H-6^b), 5.30 (t, $J_{1,2}$ = $J_{2,3}$ = 7.5 Hz, 1 H, H-2), 5.39 (t, $J_{2'',3''}$ = $J_{3'',4''}$ = 9.6 Hz, 1 H, H-3″), 5.56 (d, $J_{1'',2''}$ = 3.3 Hz, 1 H, H-1″), 5.61 (t, $J_{3,4}$ = $J_{4,5}$ = 8.4 Hz, 1 H, H-4), 6.95–8.10 (m, 35 H, 7 Ph).

MS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{72}H_{72}F_3NO_{19}$: 1334.455: found: 1334.460.

In addition, isomeric product **26β** was isolated from the mixture. Yield: 30 mg (15%).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.72 (m, 2 H, $CH_2CH_2CH_2$), 1.94 (s, 3 H, CH_3), 3.02 (dd, $J_{1',2'}$ = 3.2, $J_{2',3'}$ = 9.7 Hz, 1 H, H-2′), 3.17 (t, $J_{1'',2''} = J_{2'',3''}$ = 7.9 Hz, 1 H, H-2″), 3.20–3.64 (m, 8 H, H-4′, H-5′, H-4″, H-5$^{a''}$, CH_2CH_2NH, $OCHH'CH_2$), 3.81–4.16 (m, 7 H, H-3, H-5, H-3′, H-5$^{b''}$, $OCHH'CH_2$, $PhCH_2$), 4.40–4.75 (m, 11 H, H-1, H-6, H-1′, H-1″, 3 $PhCH_2$), 5.10 (t, $J_{2'',3''} = J_{3'',4''}$ = 9.3, 1 H, H-3″), 5.21 (t, $J_{1,2} = J_{2,3}$ = 7.1 Hz, 1 H, H-2), 5.53 (t, $J_{3,4} = J_{4,5}$ = 8.2 Hz, 1 H, H-4), 6.95–8.10 (m, 35 H, 7 Ph).

3-Aminopropyl α-D-Xylopyranosyl-(1→3)-α-D-xylopyranosyl-(1→3)-β-D-glucopyranoside (3)

Deprotection of compound **26α** (100 mg, 0.076 mmol) as described for the preparation of compound **1** gave the trisaccharide **3** as a salt with AcOH. Yield: 28 mg (66%); $[\alpha]_D$ 93 (*c* 0.5, H_2O).

^{1}H NMR (500 MHz, D_2O): δ = 1.95 (s, 3 H, CH_3), 2.03 (m, 2 H, $CH_2CH_2CH_2$), 3.16 (t, *J* = 7.0 Hz, 2 H, CH_2CH_2NH), 3.39 (t, $J_{1,2} = J_{2,3}$ = 8.0 Hz, 1 H, H-2), 3.47 (m, 1 H, H-5), 3.54 (dd, $J_{1'',2''}$ = 3.8 Hz, $J_{2'',3''}$ = 9.6 Hz, 1 H, H-2″), 3.57–3.74 (m, 8 H, H-3, H-4, H-6^a, H-2′, H-4′, H-5$^{a'}$, H-3″, H-5$^{a''}$), 3.78–3.93 (m, 6 H, H-6^b, H-3′, H-5$^{b'}$, H-5$^{b''}$, H-4″, $OCHH'CH_2$), 4.09 (m, 1 H, $OCHH'CH_2$), 4.53 (d, $J_{1,2}$ = 8.0 Hz, 1 H, H-1), 5.35 (m, 2 H, H-1′, H-1″).

^{13}C NMR (125 MHz, D_2O): δ = 28.10 ($CH_2CH_2CH_2$), 39.03 (CH_2CH_2NH), 61.95 (C-6), 62.93, 63.06 (C-5′, C-5″), 69.28 (OCH_2CH_2), 70.57, 70.84, 71.21 (C-4, C-2′, C-4′, C-4″), 72.84, 72.90 (C-2, C-2″), 74.21 (C-3″), 76.85 (C-5), 80.36 (C-3′), 83.17 (C-3), 100.21, 100.41 (C-1′, C-1″), 103.52 (C-1).

MS (MALDI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{36}NO_{14}$: 502.214; found: 502.213.

3-(Octanoylamino)propyl α-D-Xylopyranosyl-(1→3)-β-D-glucopyranoside (2)

A solution of disaccharide **1** as its acetate salt (10.0 mg, 0.023 mmol), *N*-(octanoyloxy)succinimide (6 mg, 0.026 mmol), and Et_3N (4.2 μL, 0.029 mmol) in anhyd DMF (0.4 mL) was kept for 1 h at r.t. The mixture was concentrated and the product **2** was isolated from the residue by chromatography on a Sephadex G-15 gel column. Yield: 8.1 mg (70%); $[\alpha]_D$ 37 (*c* 0.5, MeOH).

^{1}H NMR (500 MHz, D_2O): δ = 0.81 (t, *J* = 6.7 Hz, 3 H, CH_3), 1.25 (m, 8 H, 4 CH_2), 1.53, 1.77 (2 m, 4 H, 2 CH_2), 2.17 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.24 (t, *J* = 7.0 Hz, 2 H, CH_2CH_2NH), 3.30 (t, $J_{1,2} = J_{2,3}$ = 7.9 Hz, 1 H, H-2), 3.39 (m, 1 H, H-5), 3.46 (dd, $J_{1',2'}$ = 3.7 Hz, $J_{2',3'}$ = 9.3 Hz, 1 H, H-2′), 3.53–3.70 (m, 7 H, H-3, H-4, H-6^a, H-3′, H-4′, H-5$^{a'}$, $OCHH'CH_2$), 3.77–3.95 (m, 3 H, H-6^b, H-5$^{b'}$, $OCHH'CH_2$), 4.40 (d, $J_{1,2}$ = 8.0 Hz, 1 H, H-1), 5.25 (d, $J_{1',2'}$ = 3.7 Hz, 1 H, H-1′).

^{13}C NMR (125 MHz, D_2O): δ = 14.47 (CH_3), 23.01 (CH_2), 26.45 (CH_2), 29.12 (CH_2), 29.19 (CH_2), 29.54 (CH_2), 32.05 (CH_2), 36.92 (CH_2), 37.32 (CH_2), 61.70 (C-6), 62.61 (C-5′), 69.00 (OCH_2CH_2), 70.46 (C-4′), 71.24 (C-4), 72.74, 72.89 (C-2, C-2′), 74.13 (C-3′), 76.75 (C-5), 83.04 (C-3), 100.18 (C-1′), 103.50 (C-1), 178.38 ($NHCOCH_2$).

MS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{41}NO_{11}$: 518.257; found: 518.258.

3-(Octanoylamino)propyl α-D-Xylopyranosyl-(1→3)-α-D-xylopyranosyl-(1→3)-β-D-glucopyranoside (4)

Trisaccharide **3** (10.0 mg, 0.18 mmol) was N-octanoylated as described for the preparation of **2** to give neoglycolipid **4**. Yield: 8.3 mg (74%); $[\alpha]_D$ 59 (*c* 0.5, MeOH).

^{1}H NMR (500 MHz, D_2O): δ = 0.80 (t, *J* = 6.4 Hz, 3 H, CH_3), 1.22 (m, 8 H, 4 CH_2), 1.52, 1.77 (2 m, 4 H, 2 CH_2), 2.17 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.22 (t, *J* = 6.7 Hz, 2 H, CH_2CH_2NH), 3.27–3.95 (m, 18 H, H-2, H-5, H-2″, H-3, H-4, H-6, H-2′, H-4′, H-5′, H-3″, H-5″, H-3′, H-4″, OCH_2CH_2), 4.40 (d, $J_{1,2}$ = 8.0 Hz, 1 H, H-1), 5.26 (m, 2 H, H-1′, H-1″).

^{13}C NMR (125 MHz, D_2O): δ = 14.47 (CH_3), 23.01 (CH_2), 25.97 (CH_2), 26.45 (CH_2), 29.11 (CH_2), 29.53 (CH_2), 32.04 (CH_2), 36.92 (CH_2), 37.34 (CH_2), 61.68 (C-6), 62.59, 62.70 (C-5′, C-5″), 69.02 (OCH_2CH_2), 70.48, 70.79, 71.16 (C-4, C-2′, C-4′, C-4″), 72.77, 72.88 (C-2, C-2″), 74.12 (C-3″), 76.75 (C-5), 80.33 (C-3′), 83.20 (C-3), 100.13, 100.33 (C-1′, C-1″), 103.48 (C-1), 178.40 ($NHCOCH_2$).

MS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{49}NO_{15}$: 650.300; found: 650.299.

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