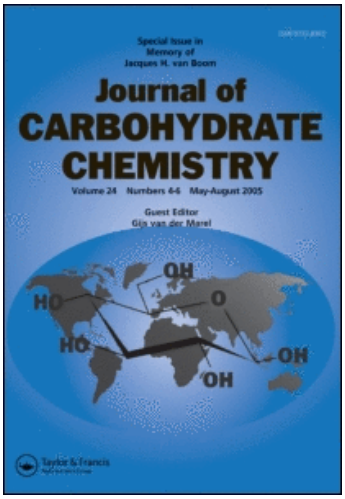

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SYNTHESIS OF A 4-DEOXY-4-*C*-METHYLENE ANALOG OF GLUCOSYLCERAMIDE

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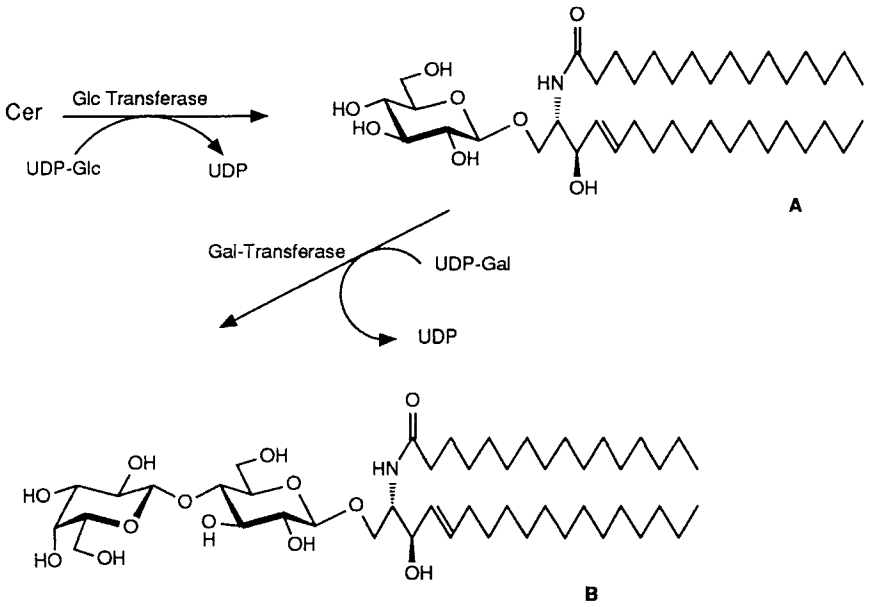
ABSTRACT

D-Glucose was transformed into 2,3:5,6-di-*O*-isopropylidene dithioacetal **1**; its oxidation to ketone **2** and subsequent Wittig reaction afforded 4-deoxy-4-*C*-methylene derivative **3**. Hydrolytic removal of the protective groups, then *O*-acetylation, selective anomeric *O*-deacetylation, and base catalyzed trichloroacetonitrile addition furnished 4-deoxy-4-*C*-methylene substituted glycopyranosyl donor **7** as an anomeric mixture. Reaction of **7** with azidosphingosine derivative **8** under BF_3·OEt_2 catalysis gave β-glycopyranoside **9**. Azido group reduction with triphenylphosphine in the presence of palmitic anhydride and water afforded directly *O*-acyl protected glycosphingolipid derivative **10** which yielded after Zemplen *O*-deacylation target molecule **11**.

INTRODUCTION

The biosynthesis of glycosphingolipids (GSL) starts from ceramides to which, with the help of activated sugars and glycosyl transferases, sugar residues are attached one by one.[1] Thus, with UDP-glucose (UDP-Glc) and glucosyl transferase glucosyl ceramide (**A**, Scheme 1) is obtained and then with UDP-galactose (UDP-Gal) and galactosyl transferase the β(1-4)-linkage is generated providing lactosyl ceramide (**B**) which is the basic constituent of various types of GSL's. Therefore, modifications of the glucosyl moiety in 4-position should provide interesting target molecules for biological testing.[2,3] Therefore, we planned to introduce at C-4 of glucose a methylene group, thus leading to gluco-

Scheme 1

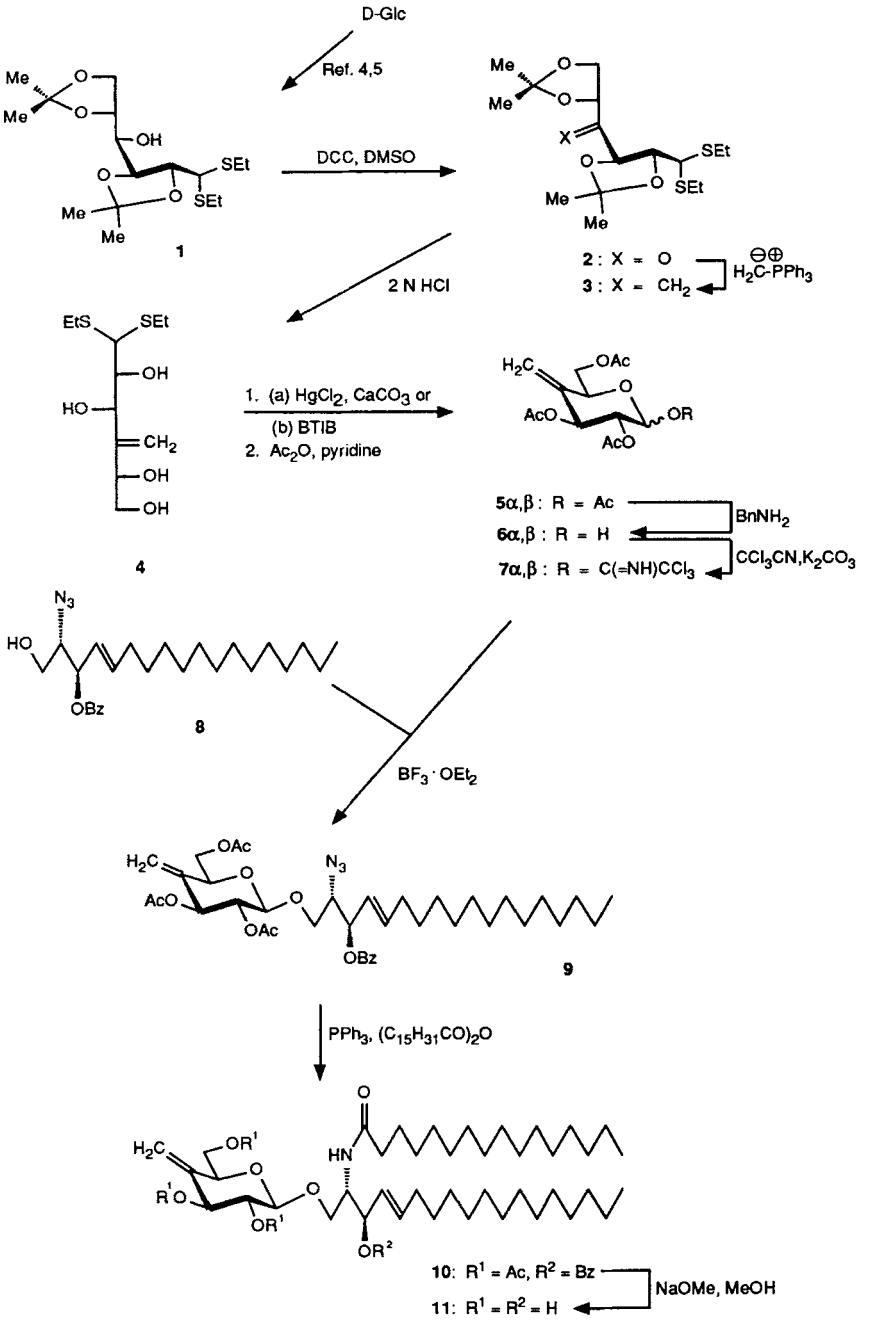


syl ceramide analog **11** (Scheme 2) as target molecule which cannot undergo galactosylation at its 4-position.[3] However, as a substrate analog of **A**, compound **11** could act as a reversible inhibitor. Alternatively, if the sugar ethylidene moiety experiences activation at the active site of the galactosyl transferase, covalent binding to the enzyme could be induced resulting in suicide inhibition of the enzyme.

RESULTS AND DISCUSSION

The strategy for the synthesis of methylene branched glucosyl ceramide analog **11** was not compatible with the common *O*-benzyl protection protocol because benzyl group removal might lead to reaction at the sugar ethylidene moiety as well. Because methylenation of *O*-acyl protected 4-ulose derivatives of glucose also caused problems,[3] acid labile acetal *O*-protective groups were employed in the required modifications. Thus, glucose was transformed into 4-*O*-unprotected ring opened dithioacetal **1** following a two step procedure published by Curtis and Jones.[4,5] Pfitzner-Moffatt[6] oxidation of **1** led to quantitative formation of ulose derivative **2**. Wittig reaction of **2** with methylene triphenylphosphorane provided the methylene branched derivative **3**. Acid catalyzed hydrolytic removal of the *O*-isopropylidene protective groups gave 2,3,5,6-*O*-unprotected

Scheme 2



compound **4** which required dithioacetal cleavage as the next step to generating the pyranose form.

However, this step turned out to be the critical,[3] and was effected by treating compound **4** with $HgCl_2$ in the presence of $CaCO_3$[7] in aqueous acetone leading to the cleavage product which was immediately transformed into the *O*-acetyl protected pyranose **5** (**5**α:**5**β = 1:3; total yield 32%). Bis(trifluoroacetoxy)iodobenzene[8] (BTIB) and several other reagents, reported for convenient dithioacetal cleavage[3] did not lead to better yields. The ^1H NMR chemical shifts observed for 5-H and 6-H of **5**α,β (and also those for the derived *O*-acetylated compounds **6**,**7**,**9**, and **10**) confirm the pyranose structure. A different approach for the synthesis of methylene branched pyranoses was reported by Depezay and Le Merrer.[9] Selective removal of the anomeric *O*-acetyl group in **5** with benzylamine[10] provided 1-*O*-unprotected compound **6** required for anomeric *O*-activation with trichloroacetonitrile in presence of K_2CO_3 as base,[11] thus furnishing the corresponding trichloroacetimidate **7** which was obtained as an anomeric mixture (**7**α:**7**β = 1:2).

For the connection of the sugar moiety with the ceramide moiety the azidosphingosine glycosylation procedure[12] was employed. Thus, reaction of **7**α,β with azidosphingosine derivative **8**[13] in the presence of boron trifluoride diethyl ether as catalyst furnished, due to neighboring group participation, exclusively the β-connected glycoside **9**. Azide group reduction and *N*-palmitoylation was performed as a one pot reaction with triphenylphosphine and palmitic anhydride in presence of water[14] providing the *O*-acyl protected target molecule **10** in good yield. *O*-Deacylation was carried out by treatment with sodium methoxide in methanol (Zemplen conditions), thus affording the desired C-4 modified glucosyl ceramide analog **11**.[15]

EXPERIMENTAL

General methods. Solvents were purified in the usual way; petroleum ether had a boiling range of 35-70 °C. ^1H NMR spectra: Bruker WM 250 Cryospec; solvents $CDCl_3$ and [D_6]DMSO; internal standard tetramethylsilane (TMS). Column chromatography: Merck silica gel 60, 0.063-0.200 mm. Flash chromatography: silica gel (Baker, 30-60 μm). Medium pressure liquid chromatography (MPLC): Merck silica gel LiChroprep Si 60, 15-25 μm. Thin-layer chromatography (TLC): Merck plates, silica gel 60 F_{254}, layer thickness 0.2 mm. Detection by treatment with a solution of 15% H_2SO_4, followed by heating at 120 °C. Optical rotations: Perkin-Elmer polarimeter 241/MS; 1-dm cell.

2,3:5,6-Di-*O*-isopropylidene-D-*xylo*-4-hexosulose diethyl dithioacetal (2). To a solution of **1**[4,5] (16.9 g, 46 mmol), dicyclohexylcarbodiimide (28.5 g, 138 mmol), dry

dimethyl sulfoxide (17.6 g, 225 mmol) and dry pyridine (3 mL) in dry diethyl ether (250 mL) at 0 °C was added dropwise trifluoroacetic acid (3 mL). The mixture was stirred for 3.5 h at room temperature and cooled to 0 °C. Oxalic acid dihydrate (23 g, 182 mmol) was added in several portions. After stirring for one additional hour at room temperature the mixture was filtered through Celite. The filtrate was worked up with saturated sodium hydrogen carbonate solution (4 x 100 mL), dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by chromatography [petroleum ether-ethyl acetate (9:1)] to give **2** (16.0 g, quant.) as a pale yellow oil; TLC [petroleum ether-ethyl acetate (9:1)]: R_F 0.58, $[\alpha]_D^{20}$ -27 (*c* 2, chloroform); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.25, 1.27 (2 t, J = 7.4 Hz, 6H, C*H*$_3$-CH$_2$-S), 1.34, 1.43, 1.48, 1.51 (4 s, 12H, 4 CH$_3$ [isopropylidene)], 2.67 - 2.76 (m, 4H, 2 CH$_3$-C*H*$_2$-S), 4.01 (d, $J_{1,2}$ = 5.0 Hz, 1H, 1-H), 4.12 (dd, $J_{5,6}$ = 5.7 Hz, $J_{6,6'}$ = 8.7 Hz, 1H, 6-H), 4.28 (dd, $J_{5,6'}$ = 7.5 Hz, $J_{6,6'}$ = 8.7 Hz, 1H, 6'-H), 4.59 (dd, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 7.0 Hz, 1H, 2-H), 4.76 (d, $J_{2,3}$ = 7.0 Hz, 1H, 3-H), 4.90 (dd, $J_{5,6}$ = 5.7 Hz, $J_{5,6'}$ = 7.5 Hz, 1H, 5-H).

Anal. Calcd for $C_{12}H_{28}O_5S_2$: C, 52.72; H, 7.74. Found: C, 52.99; H, 7.60.

4-Deoxy-2,3:5,6-di-*O*-isopropylidene-4-*C*-methylene-D-*xylo*-hexose diethyl dithioacetal (3). To a suspension of methyltriphenylphosphonium bromide (30.4 g, 85 mmol) in dry tetrahydrofuran (300 mL) under a nitrogen atmosphere, *n*-butyllithium (85 mmol, 53 mL of a 1.6 M solution in hexane) was added dropwise with stirring. The mixture was stirred for 2.5 h at room temperature. A solution of **2** (15.5 g, 42.5 mmol) in dry tetrahydrofuran (50 mL) was added dropwise. After 2 h the mixture was poured into saturated ammonium chloride solution (150 mL) and extracted with diethyl ether (3 x 100 mL). The combined extracts were washed with brine (150 mL), dried over sodium sulfate and concentrated *in vacuo*. The residue was chromatographed [petroleum ether-ethyl acetate (9:1)] to give **3** (10.3 g, 67%) as a pale yellow oil; TLC [petroleum ether-ethyl acetate (9:1)]: R_F 0.48, $[\alpha]_D^{22}$ -25 (*c* 1, chloroform); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.26, 1.27 (2 t, J = 7.5 Hz, 6H, C*H*$_3$-CH$_2$-S), 1.42, 1.43 [2 s, 6H, 2 CH$_3$(isopropylidene)], 1.46 [2 s, 6H, 2 CH$_3$ (isopropylidene)], 2.67 - 2.80 (m, 4H, 2 CH$_3$-C*H*$_2$-S), 3.70 (dd, $J_{5,6}$ = 8.0 Hz, $J_{6,6'}$ = 8.1 Hz, 1H, 6-H), 3.94 (d, $J_{1,2}$ = 3.7 Hz, 1H, 1-H), 4.20 (dd, $J_{5,6'}$ = 6.1 Hz, $J_{6,6'}$ = 8.1 Hz, 1H, 6'-H), 4.21 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 8.0 Hz, 1H, 2-H), 4.60 (bd, $J_{2,3}$ = 8.0 Hz, 1 H, 3-H), 4.58 - 4.65 (m, 1H, 5-H), 5.35, 5.51 (2 bs, 2H, C=CH$_2$).

Anal. Calcd for $C_{17}H_{30}O_4S_2$: C, 56.32; H, 8.34. Found: C, 56.36; H, 8.29.

4-Deoxy-4-*C*-methylene-D-*xylo*-hexose diethyl dithioacetal (4). To a solution of **3** (9.63 g, 26.4 mmol) in tetrahydrofuran (30 mL) was added 2 N hydrochloric acid (30 mL). The mixture was stirred for 72 h at room temperature and extracted with chlo-

roform (10 x 20 mL). The combined organic extracts were dried over magnesium sulfate and concentrated *in vacuo*. Chromatography (ethyl acetate) yielded **4** (5.44 g, 72%) as an amorphous solid; TLC (ethyl acetate): R_F 0.30, $[\alpha]_D^{22}$ +53 (*c* 1, chloroform); ^1H NMR (250 MHz, $CDCl_3$) δ 1.27, 1.28 (2 t, J = 7.4 Hz, 6H, CH_3-CH_2-S), 2.68 - 2.75 (m, 4H, 2 CH_3-CH_2-S), 3.56 (m, 4H, 4 OH), 3.71 - 3.78 (m, 3H, 2-H, 2 6-H), 4.03 (d, $J_{1,2}$ = 7.3 Hz, 1H, 1-H), 4.40 (bdd, $J_{5,6}$ = 4.6 Hz, $J_{5,6'}$ = 10.0 Hz, 1H, 5-H), 4.39 (bd, $J_{2,3}$ = 4.7 Hz, 1H, 3-H), 5.28, 5.30 (2 bs, 2H, C=CH_2).

Anal. Calcd for $C_{11}H_{22}O_4S_2$: C, 46.78; H, 7.85. Found: C, 46.84; H, 7.91.

1,2,3,6-Tetra-*O*-acetyl-4-deoxy-4-*C*-methylene-D-*xylo*-hexopyranose (5).

Procedure (a): To a solution of **4** (7.9 g, 27.9 mmol) in 95% aqueous acetone (50 mL) was added mercuric chloride (16.6 g, 61.2 mmol) and calcium carbonate (16.6 g). The mixture was stirred for 24 h at room temperature, filtered through calcium carbonate and concentrated under reduced pressure (water bath temperature < 20 °C). Dry pyridine (50 mL) and dry acetic anhydride (50 mL) were added at 0 °C to the residue, and the mixture was shaken at room temperature for 2 h and then concentrated at 10^{-2} Torr. The residue is dissolved in chloroform and extracted with 1 M potassium iodide solution (20 mL). The organic solution was dried over sodium sulfate and concentrated under reduced pressure. Chromatography [petroleum ether-ethyl acetate (6:4)] gave **5** (3.1 g, 32%) as a colourless syrup.

Procedure (b): To a solution of **4** (8.36 g, 29.3 mmol) in 90% aqueous acetonitrile at 0 °C was added with stirring [bis(trifluoracetoxy)iodo]benzene (12.6 g, 29.3 mmol) in several portions. After 10 min, pyridine (15 mL) was added dropwise and the mixture was concentrated *in vacuo*. Dry pyridine (50 mL) and dry acetic anhydride (50 mL) were added to the residue at 0 °C. After 2 h at room temperature the mixture was concentrated at 10^{-2} Torr. Chromatography [petroleum ether-ethyl acetate (6:4)] gave **5** [3.29 g, 33%; α:β = 1:3 (on the basis of ^1H NMR)]. TLC [petroleum ether-ethyl acetate (1:1)]: R_F 0.48; ^1H NMR (250 MHz, $CDCl_3$) of the anomeric mixture: **5**α: δ 2.07, 2.09, 2.11, 2.14 (4 s, 12H, 4 OAc), 4.32 - 4.46 (m, 2H, 2 6-H), 4.69 (m, 1H, 5-H), 5.03 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.0 Hz, 1H, 2-H), 5.09, 5.13 (2 bs, 2H, C=CH_2), 5.78 (bd, $J_{2,3}$ = 10.0 Hz, 1H, 3-H), 6.38 (d, $J_{1,2}$ = 3.7 Hz, 1H, 1-H). **5**β: δ = 2.03, 2.05, 2.16, 2.18 (4 s, 12H, 4 OAc), 4.32 - 4.46 (m, 3H, 5-H, 2 6-H), 5.02 (dd, $J_{1,2}$ = 6.7 Hz, $J_{2,3}$ = 8.2 Hz, 1H, 2-H), 5.16, 5.21 (2 bs, 2H, C=CH_2), 5.60 (bd, $J_{2,3}$ = 8.2 Hz, 1H, 3-H), 5.84 (d, $J_{1,2}$ = 6.7 Hz, 1H, 1-H).

Anal. Calcd for $C_{15}H_{20}O_9$: C, 52.32; H, 5.85. Found: C, 52.08; H, 5.99.

2,3,6-Tri-*O*-acetyl-4-deoxy-4-*C*-methylene-D-*xylo*-hexopyranose (6). To a solution of **5** (500 mg, 1.45 mmol) in dichloromethane was added benzylamine (0.47 mL,

0.49 g, 4.6 mmol). After 16 h at room temperature the mixture was diluted with 1 N hydrochloric acid (4.6 mL) and extracted with dichloromethane (3 x 10 mL). The combined organic extracts were washed with saturated sodium hydrogen carbonate solution (20 mL), dried over magnesium sulfate and concentrated under reduced pressure. Chromatography [petroleum ether-ethyl acetate (6:4)] gave **6** [210 mg, 48%; α:β = 7:3 (on the basis of ^{1}H NMR)] as a colourless foam. TLC [petroleum ether-ethyl acetate (6:4)]: benzylamine/**5**-intermediate: R_F 0.48; **6**: R_F 0.37; ^{1}H NMR (250 MHz, $CDCl_3$) of the anomeric mixture: δ 2.10, 2.11, 2.15 (3 s, 9H, 3 OAcα, 3 OAcβ), 3.26 (bs, 0.7H, OHα), 3.68 (bs, 0.3H, OHβ), 4.20 - 4.24 (m, 0.3H, 5-Hβ), 4.29 - 4.50 (m, 2H, 2 6-Hα, 2 6-Hβ), 4.71 - 4.90 (m, 1.3H, 1-Hβ, 2-Hβ, 5-Hα), 4.87 (dd, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.1 Hz, 0.7H, 2-Hα), 5.03 - 5.16 (m, 2H, C=CH_2α, C=CH_2β), 5.48 - 5.51 (m, 1H, 1-Hα, 3-Hβ), 5.82 (bd, $J_{2,3}$ = 10.1 Hz, 0.7H, 3-Hα).

Anal. Calcd for $C_{13}H_{18}O_8$: C, 51.68; H, 5.96. Found: C, 51.61; H, 6.03.

***O*-(2,3,6-Tri-*O*-acetyl-4-deoxy-4-*C*-methylene-D-*xylo*-hexopyranosyl)-trichloroacetimidate** (**7**). A mixture of **6** (440 mg, 1.45 mmol), trichloroacetonitrile (0.3 mL, 430 mg, 3.0 mmol) and potassium carbonate (150 mg) in dry dichloromethane (5 mL) was stirred for 16 h at room temperature and filtered through Celite. Flash chromatography [Florisil (200-300 mesh ASTM), petroleum ether-ethyl acetate (7:3)] yielded **7** [540 mg, 83%; α:β = 1:2 (on the basis of ^{1}H NMR)] as a colourless foam. TLC [petroleum ether-ethyl acetate (7:3)]: **7**α: R_F 0.41; **7**β: R_F 0.26; ^{1}H NMR (250 MHz, $CDCl_3$) of the anomeric mixture: **7**α: δ 2.07, 2.08, 2.14 (3 s, 9H, 3 OAc), 4.29 - 4.58 (m, 2H, 2 6-H), 4.70 (m, 1H, 5-H), 5.08 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.7 Hz, 1H, 2-H), 5.11, 5.14 (2 bs, 2H, 2 C=CH_2), 5.85 (bd, $J_{2,3}$ = 10.7 Hz, 1H, 3-H), 6.60 (d, $J_{1,2}$ = 3.7 Hz, 1H, 1-H), 8.66 (s, 1H, 1 NH). **7**β: δ = 2.03, 2.06, 2.17 (3 s, 9H, 3 OAc), 4.29 - 4.58 (m, 3H, 5H, 2 6-H), 5.19 (dd, $J_{1,2}$ = 4.8 Hz, $J_{2,3}$ = 7.4 Hz, 1H, 2-H), 5.27, 5.31 (2 bs, 2H, C=CH_2), 5.50 (d, $J_{2,3}$ = 7.4 Hz, 1H, 3-H), 6.08 (d, $J_{1,2}$ = 4.8 Hz, 1H, 1-H), 8.66 (s, 1H, 1 NH).

(2*S*,3*R*,4*E*)-2-Azido-3-benzoyloxy-1-(2,3,6-tri-*O*-acetyl-4-deoxy-4-*C*-methylene-β-D-*xylo*-hexopyranosyloxy)-4-octadecene (**9**). The anomeric mixture of α/β-trichloroacetimidate **7** (560 mg, 1.21 mmol) and **8** (520 mg, 1.21 mmol) was dissolved in dry *n*-hexane (3 mL) and dry dichloromethane (1 mL). The solution was stirred at room temperature under a nitrogen atmosphere in the presence of molecular sieves (4Å, 100 mg) for 10 min. Diethyl ether-boron trifluoride (0.6 mL of a 0.2 M solution in dry dichloromethane) was added dropwise and stirring was continued for 2.5 h. The mixture was diluted with petroleum ether (60 mL) and extracted with a saturated sodium hydrogen carbonate solution (3 x 10 mL). Flash chromatography [petroleum ether-ethyl acetate (8:2)] yielded **9** (470 mg, 55%; turnover, 63%) and glycosyl acceptor **8** (70 mg).

TLC [petroleum ether-ethyl acetate (7:3)]: R_F 0.52, $[\alpha]_D^{22}$ -39 (*c* 1, chloroform); ^1H NMR (250 MHz, $CDCl_3$) δ 0.85 (t, J = 6.4 Hz, 3H, CH_3), 1.21 - 1.36 (m, 22H, 11 CH_2), 2.00 - 2.11 (m, 2*H*, CH=CH-C*H*$_2$), 2.03, 2.10, 2.14 (3 s, 9H, 3 OAc), 3.59 (dd, J = 4.8 Hz, J = 9.2 Hz, 1H, CH_2O), 3.84 - 3.96 (m, 2H, C*H*$_2$O, C*H*-N_3), 4.16 - 4.21 (m, 1H, 5-H), 4.30 (dd, $J_{5,6}$ = 8.8 Hz, $J_{6,6'}$ = 11.4 Hz, 1H, 6-H), 4.40 (dd, $J_{5,6'}$ = 4.8 Hz, $J_{6,6'}$ = 11.4 Hz, 1H, 6'-H), 4.63 (d, $J_{1,2}$ = 6.7 Hz, 1H, 1-H), 4.95 (dd, $J_{1,2}$ = 6.7 Hz, $J_{2,3}$ = 8.5 Hz, 1H, 2-H), 5.11, 5.16 (2 bd, J_{gem} = 1.2 Hz, 2H, C=CH_2), 5.45 (bd, $J_{2,3}$ = 8.5 Hz, 1H, 3-H), 5.53 - 5.61 (m, 2H, C*H*=CH-CH_2, CH-OBz), 5.93 (dt, J = 6.7 Hz, J = 14.3 Hz, 1H, CH=C*H*-CH_2), 7.42 - 7.48 (m, 2H, Ph), 7.54 - 7.57 (m, 1H, Ph), 8.03- 8.07 (m, 2H, Ph).

Anal. Calcd for $C_{38}H_{55}N_3O_{10}$: C, 63.93; H, 7.77; N, 5.88. Found: C, 63.94; H, 7.65; N, 5.68.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-(2,3,6-tri-*O*-acetyl-4-deoxy-4-*C*-methylene-β-D-*xylo*-hexopyranosyloxy-4-octadecene (10). Triphenylphosphine (150 mg, 0.57 mmol), hexadecanoic anhydride (340 mg, 0.68 mmol) and **9** (307 mg, 0.43 mmol) were dissolved in dry tetrahydrofuran (5 mL). After 36 h at room temperature water (0.2 mL) was added. After 48 h, the mixture was concentrated under reduced pressure and co-evaporated with pyridine (1 x 20 mL) and toluene (2 x 20 mL). Flash chromatography [petroleum ether-ethyl acetate (7:3)] and lyophilization from dioxan yielded **10** (266 mg, 67%) as a colourless powder. TLC [petroleum ether-ethyl acetate (7:3)]: R_F 0.36, $[\alpha]_D^{22}$ +1.8 (*c* 10, chloroform); ^1H NMR (250 MHz, $CDCl_3$) δ 0.88 (2 t, J = 6.8 Hz, 6H, 2 CH_3), 1.11 - 1.45 (m, 46H, 23 CH_2), 1.57 -1.59 (m, 2H, CH_2), 1.90, 2.05, 2.14 (3 s, 9H, 3 OAc), 2.00 - 2.18 (m, 4H, CH=CH-C*H*$_2$, NCO-CH_2), 3.62 (dd, J = 4.0 Hz, J = 10.1 Hz, 1H, C*H*$_2$O), 4.06 (dd, J = 3.9 Hz, J = 10.1 Hz, 1H, C*H*$_2$O), 4.17 - 4.22 (m, 2H, 5-H, 6-H), 4.35 (dd, $J_{5,6}$ = 7.4 Hz, $J_{6,6'}$ = 10.6 Hz, 1H, 6'-H), 4.45 - 4.51 (m, 1H, CHN), 4.57 (d, $J_{1,2}$ = 6.6 Hz, 1 H, 1-H), 4.87 (dd, $J_{1,2}$ = 6.6 Hz, $J_{2,3}$ = 8.7 Hz, 1H, 2-H), 5.08, 5.13 (2 bd, J_{gem} = 1.5 Hz, 2H, C=CH_2), 5.43 (d, $J_{2,3}$ = 8.7 Hz, 1H, 3-H), 5.42 - 5.58 (m, 2H, C*H*=CH-CH_2, CH-OBz), 5.81 - 5.92 (m, 2H, CH=C*H*-CH_2, NH), 7.40 - 7.46 (m, 2H, Ph), 7.53 - 7.58 (m, 1H, Ph), 8.00 - 8.04 (m, 2H, Ph).

Anal. Calcd for $C_{53}H_{87}NO_{11}$: C, 69.63; H, 9.59; N, 1.53. Found: C, 69.89; H, 9.35; N, 1.62.

(2*S*,3*R*,4*E*)-1-(4-Deoxy-4-*C*-methylene-β-D-*xylo*-hexopyranosyloxy)-2-hexadecanoylamino-4-octadecen-3-ol (11). To a solution of **10** (232 mg, 0.25 mmol) in dry dichloromethane (2 mL) was added sodium methanolate (0.7 mL of a 0.1 N solution in methanol). After 3 h at room temperature the mixture was diluted with chloroform (5 mL), neutralized with ion exchange resin (Amberlite IR-120, H^+) and filtered. The filtrate was concentrated under reduced pressure. Flash chromatography

[chloroform/methanol (9:1)] and lyophilization from dioxane yielded **11** (151 mg, 87%) as a colourless powder. TLC [chloroform/methanol (9:1)]: R_F 0.30, $[\alpha]_D^{22}$ -5 (*c* 1, pyridine); ^{1}H NMR (250 MHz, [D_6]DMSO) δ 0.85 (2 t, J = 6.7 Hz, 6H, 2 CH_3), 1.23 (m, 46H, 23 CH_2), 1.44 (m, 2H, CH_2), 1.92 - 2.05 (m, 4H, CH=CH-CH_2, NCO-CH_2), 3.41 - 3.99 (m, 8H, 3-H, 5-H, 2 6-H, 2 CH_2O, CHN, CHO), 4.24 (d, $J_{1,2}$ = 7.6 Hz, 1H, 1-H), 4.70 (d, J = 5.2 Hz, 1H, OH), 4.89 (d, J = 5.4 Hz, 1H, OH), 4.93, 5.13 (2 bs, 2H, C=CH_2), 5.21 (d, J = 3.7 Hz, 1H, OH), 5.24 (d, J = 5.5 Hz, 1H, OH), 5.35 (dd, J = 7.0 Hz, J = 15.3 Hz, 1H, C*H*=CH-CH_2), 5.52 (dt, J = 6.4 Hz, J = 15.3 Hz, 1H, CH=C*H*-CH_2), 7.50 (d, J = 8.7 Hz, 1H, NH); ^{1}H NMR [250 MHz, $CDCl_3$/CD_3OD (9:1)] : δ = 0.88 (2 t, J = 6.5 Hz, 6 H, 2 CH_3), 1.01 - 1.39 (m, 46 H, 23 CH_2), 1.59 (m, 2H, CH_2), 1.97 - 2.03 (m, 2 H, CH=CH-CH_2), 2.13- 2.20 (m, 2 H, NCO-CH_2), 3.21 (dd, $J_{1,2}$ = 7.6 Hz, $J_{2,3}$ = 9.3 Hz, 1 H, 2-H), 3.64 (dd, J = 3.3 Hz, J = 10.1 Hz, CH_2O), 3.79 - 4.19 (m, 7 H, 3-H, 5-H, 2 6-H, CH_2O, CHN, CHO), 4.38 (d, $J_{1,2}$ = 7.6 Hz, 1-H), 4.97, 5.34 (2 bd, J_{gem} = 1.9 Hz, 2 H, 2 C=CH_2), 5.45 (dd, J = 7.3 Hz, J = 15.3 Hz, C*H*=CH-CH_2), 5.70 (dt, J = 6.4 Hz, J = 15.3 Hz, 1H, CH=C*H*-CH_2).

Anal. Calcd for $C_{41}H_{77}NO_7$: C, 70.74; H, 11.15; N, 2.01. Found: C, 70.58; H, 11.10; N, 2.35.

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