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TETRAHEDRON

Synthesis of Analogs of 1,1-Linked Galactosyl Mannoside as Mimetics of Sialyl Lewis X Tetrasaccharide

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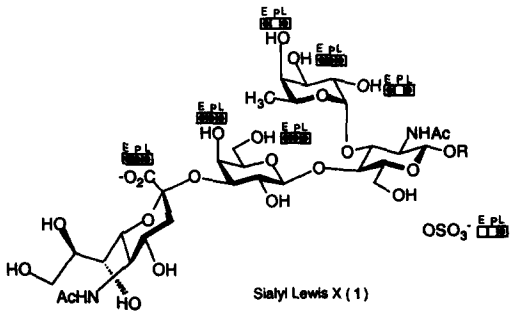
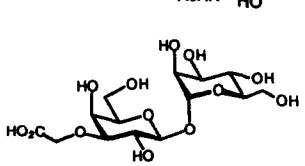
Abstract: Methods have been developed for the incorporation of hydrophobic groups with and without positive or negative charge to position-6 of the mannose residue in the 1,1-linked disaccharide as mimetics of sialyl Lewis X tetrasaccharide in order to enhance binding affinity to selectins.

INTRODUCTION

The tetrasaccharide structure **1** known as sialyl Lewis X (SLe^X) is found at the nonreducing end of glycoconjugates and is expressed on the surface of neutrophils and tumor cells. The structure has been shown to be responsible for the first stage of adhesion process in inflammatory reactions, i.e. the rolling of leukocytes along the surface of blood vessel.[1] After initial synthesis of the natural form of the tetrasaccharide on large scales as potential anti-inflammatory agent,[2] we became interested in the development of SLe^X mimetics in order to improve the stability and oral activity.[3]





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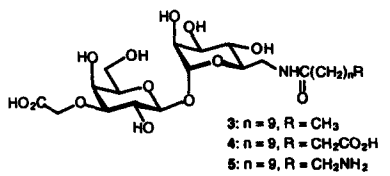

3: n = 9, R = CH_3
4: n = 9, R = CH_2CO_2H
5: n = 9, R = CH_2NH_2
6: n = 4, R = CH_2OSO_3H

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During the course of our investigation to synthesize SLe^X mimetics,[3-d,e,g-l,p-r,x] we have designed and synthesized a novel 1,1-linked disaccharide **2** [3-g], which contains all functional groups necessary for the SLe^X—E / P-selectin binding[4] in the correct through-space orientation in the bound conformation.[5] Encouraged by the result that compound **2** showed five times as strong as SLe^X in E-selectin inhibition, we have decided to develop a method for the modification of position-6 of the mannose residue in the 1,1-linked disaccharide in order to enhance binding affinity. This decision came from the analysis of the crystal structure of recombinant E-selectin[6] which contains a hydrophobic group near the C-6 position of mannose. Incorporation of a hydrophobic group into SLe^X analogs and mimetics indeed has been shown to improve inhibition potencies.[3-l,q,u,7,8] Also, to examine the possibility of enhancing the affinity by ionic interaction, charged functions such as carboxylic acid and amine were incorporated. The sulfated compound was also included as an attempt to obtain specific inhibitor of L-selectin.

We describe herein the synthesis of derivatives **3-6** of compound **2**, in which an amino group was introduced to the 6-position of the mannose residue for further modification.

RESULTS AND DISCUSSIONS

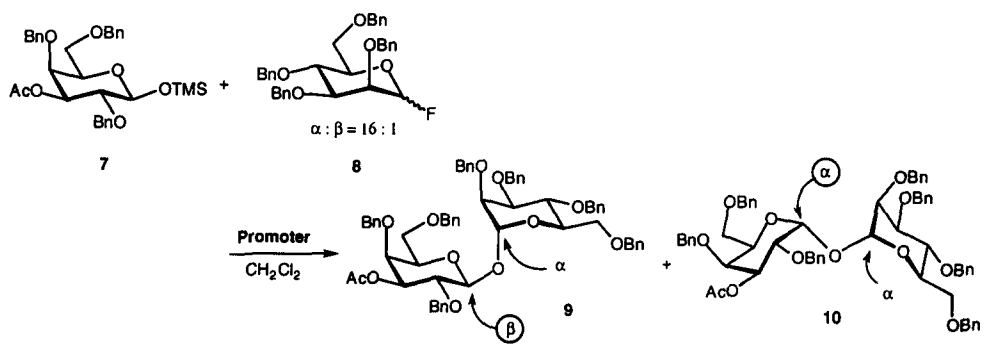


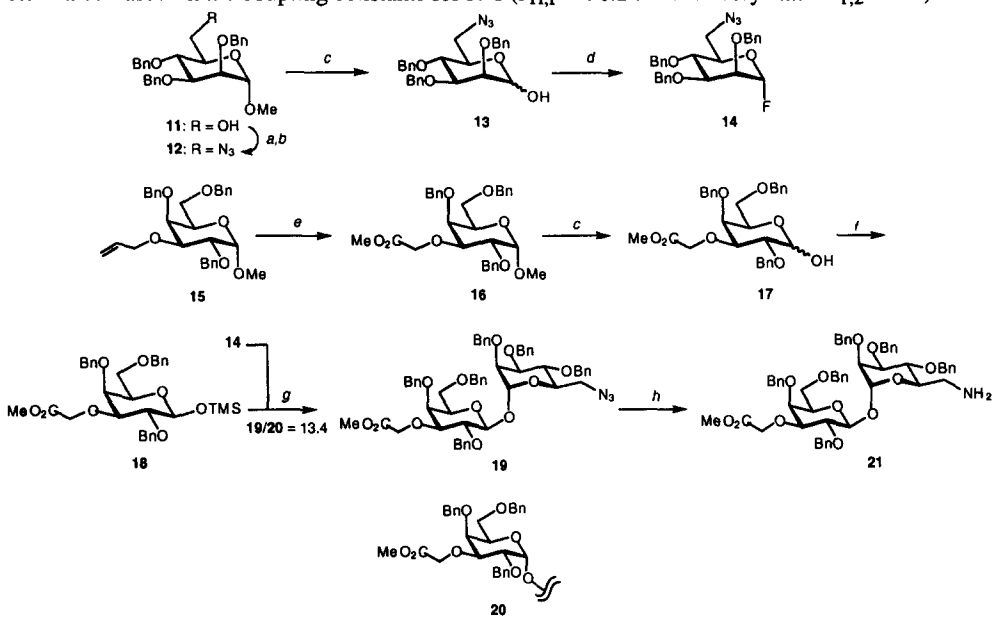
TABLE 1.

Entry	Promoter (equiv.)	Temp. / Time (°C / h)	Product (Yield ; %) 9	10	Total
1	$BF_3 \cdot OEt_2$ (0.6)	- 50 / 21	68	16	84
2	Cp_2HfCl_2 (1.2) - $AgClO_4$ (2.4)	- 78 / 3.5 ⟶ - 60 / 1.5	87	Trace	87

The key reaction in the syntheses is the 1,1-linked glycosidic linkage formation. Previously, we described the efficient synthesis of the structure using a glycosyl acceptor, of which the configuration of the anomeric oxygen was fixed as TMS glycoside and a glycosyl fluoride was used as the donor. In this reaction, we have observed formation of the anomeric mixtures due to anomerization of the TMS glycoside during the coupling reaction in the presence of borontrifluoride etherate. (Table 1, Entry 1) We therefore first re-examined, in a model study, the glycosylation reaction using glycosyl acceptor **7** and donor **8**. After several attempts, the best result obtained regarding both the yield and stereoselectivity was that using Suzuki's conditions.[9] (Table 1, Entry 2) The high

selectivity was perhaps due to the lower temperature used in the coupling reaction which prevented the anomerization of TMS glycoside leading to the exclusive formation of β-Gal-(1-1)-α-Man disaccharide **9** in 87% yield. We thus decided to use this condition for further glycosylation reactions.

The synthesis of the 6-modified mannosyl donor is as follows. The 6-hydroxyl group of the readily available methyl mannoside derivative **11** was converted to the azide group through tosylate. Acetolysis of compound **12** followed by Zémplen deacetylation gave the hemiacetal **13**, which was then transformed into the fluoride **14** using diethylaminosulfurtrifluoride (DAST). The α-configuration of the fluorinated structure was determined based on the coupling constants for H-1 ($J_{H,F}$ = 50.2 Hz with very small $J_{1,2}$ value).

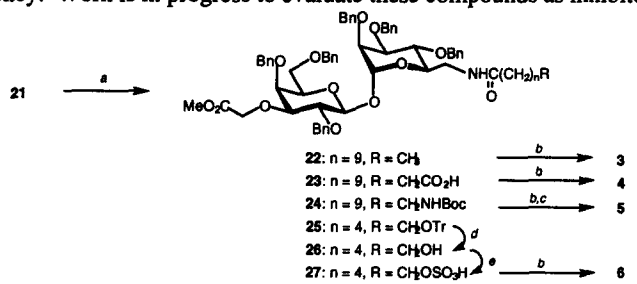


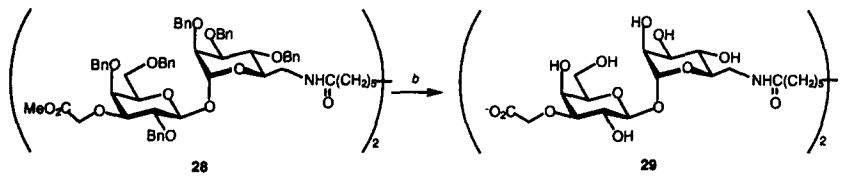
a TsCl-Et_3N; *b* NaN_3 / DMF; *c* 1) Ac_2O, H^+ / AcOH, 2) NaOMe / MeOH; *d* DAST / CH_2Cl_2; *e* 1) O_3 / MeOH then Me_2S, 2) Br_2 / 90 % aq. MeOH; *f* $TMSNEt_2$ / Toluene; *g* Cp_2HfCl_2, $AgClO_4$ / CH_2Cl_2; *h* PPh_3 / MeOH.

The galactosyl acceptor **18** was synthesized from methyl 3-*O*-allyl galactoside **15**[10]. At first, the allyl group of **15** was converted to the ether linked 2-hydroxyacetic acid methyl ester *via* ozonolysis followed by oxidation with Br_2. Acetolysis and deacetylation of compound **16** afforded **17**. Silylation of **17** with *N*-(trimethylsilyl) diethylamine resulted in the stereoselective formation of β-TMS glycoside **18** ($J_{1,2}$ = 7.3 Hz).

The coupling reaction of compounds **14** and **18** in the presence of hafnocene dichloride (Cp_2HfCl_2) and silver perchlorate ($AgClO_4$) afforded the desired disaccharide **19** (**19/20** = 13.4). Compound **19** was then converted to amine **21** by treatment with triphenylphosphine.The amine was then coupled with various carboxylic acids such as undecanoic (Laulic) acid, 1,10-decandicarboxylic acid, 12-butoxycarbonylamino (BocN)-dodecanoic acid, and 6-trityloxy-hexanoic acid in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide HCl (WSCI). The coupling reactions proceeded smoothly to yield condensates **22**, **24** and **25**, except in the coupling of dicarboxylic acid which gave the desired product **23** and the dimer **28** as a byproduct. Because the dimeric compound could be an inhibitor, we did not optimize the reaction conditions. Compound **25** was converted to sulfate **27** by hydrolysis and sulfation.

Compounds **22**, **23**, **27**, and **28** were finally hydrogenated in the presence of $Pd(OH)_2$ followed by saponification to yield **3**, **4**, **6**, and **29**, respectively. Boc-protected **24** was also deprotected through hydrogenolysis, saponification, and hydrolysis into amine **5**. We have thus established a useful method for the further modification of the bioactive SLe^X mimetic **2** in order to exploit additional binding to enhance the inhibition potency. Work is in progress to evaluate these compounds as inhibitors of selectins.





*a*Fatty acid, WSCI / CH_2Cl_2,; *b* H_2-$Pd(OH)_2$ / MeOH then aq. NaOH; *c* TFA / MeOH; *d* 80% AcOH; *e* SO_3-Pyr. / DMF.

EXPERIMENTAL

General methods

Dried solvents were used for all reactions. Solutions were evaporated under low pressure at a bath temperature not exceeding 50°C. Column chromatography was performed on silica gel (Merck Kieselgel 60). Gel permeation chromatography was performed using Bio Gel P-2. Melting points were measured with Yanaco MP-S3 micro melting point apparatus. Optical rotations were measured in a 1.0 dm tube with a Horiba SEPA-200 polarimeter at 23±1°C. ^1H NMR (270 MHz) and ^{13}C NMR (67.5 MHz) spectra were recorded with a JEOL EX-270 spectrometer in $CDCl_3$ or D_2O, unless stated otherwise, using Me_4Si (δ 0.00) as the internal standard for solutions in $CDCl_3$, or DOH (δ 4.80 at 25°C for ^1H-NMR) or using dioxane-d_8 (external, δ 67.4 for ^{13}C NMR) for solutions in D_2O. Some key compounds were measured with JEOL 400 MHz spectrometer as indicated. The FAB mass spectra were recorded using Finnigan MAT TSQ 700 equipped with a FAB ion source. Glycerol was used as the matrix.

Methyl 6-azido-6-deoxy-2,3,4-tri-O-benzyl-α-D-mannopyranoside (12)

To a solution of methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (**11**, 1.18 g, 2.4 mmol) in dichloromethane (CH_2Cl_2, 10 ml) was added triethylamine (Et_3N, 1.7 ml, 12 mmol), TsCl (2.29 g, 12 mmol) and the solution was stirred at r.t. for 3 h. Chloroform ($CHCl_3$) was added, and the solution was successively washed with aq. $NaHCO_3$ and water, dried over Na_2SO_4, evaporated and purified on a column of silica gel with hexane-ethyl acetate (EtOAc) (5:1) to give methyl 2,3,4-tri-*O*-benzyl-6-*O*-tosyl-α-D-mannopyranoside (1.47 g). The

tosylate was treated with sodium azide (NaN_3, 771 mg, 11.9 mmol) in *N,N*-dimethylformamide (6 ml) for 4 h at 90°C. The reaction mixture was diluted with Et_2O and washed with water, dried over Na_2SO_4, evaporated and purified on a column of silica gel with hexane-EtOAc (10 : 1) to give **12** (1.08 g, 93 %); $[\alpha]_D$ = +49.1° (*c* = 1.25, $CHCl_3$); ^1H NMR δ 7.44-7.14 (m, 15H, 3 Ph), 4.95, 4.48 (ABq, *J* = 11.4 Hz, PhCH_2), 4.76, 4.71 (ABq, *J* = 12.5 Hz, PhCH_2), 4.73 (brs, H-1), 4.61 (s, 2H, PhCH_2), 3.92-3.83 (m, 1H, H-3), 3.85 (t, *J* = 8.9 Hz, H-4), 3.79 (brt, H-2), 3.73 (ddd, H-5), 3 .47 (dd, $J_{5,6a}$ = 3.0 Hz, J_{gem} = 12.9 Hz, H-6a), 3.41 (dd, $J_{5,6b}$ = 6.1 Hz, H-6b), 3.34 (s, 3H, OMe); ^{13}C NMR δ 138.26, 138.17, 138.13 (Ph), 128.36-127.58 (Ph), 98.56 (C-1), 80.01 (C-3), 75.17, 72.72, 71.99 (PhCH_2), 75.40, 74.32, 71.48 (C-2,4,5), 54.90 (OMe), 51.47 (C-6).
Anal. Calcd. For $C_{28}H_{31}N_3O_5$: C, 68.69; H, 6.38; N, 8.58. Found: C, 68.45; H, 6.41; N, 8.55.

*6-Azido-2,3,4-tri-*O*-benzyl-6-deoxy-D-mannopyranose (13)*
To a solution of **12** (1.02 g, 2.09 mmol) in acetic anhydride (Ac_2O, 4 ml) was added acetic acid (AcOH, 3.8 ml), and AcOH-H_2SO_4 (500:1, 3.3 ml) dropwise then the mixture was stirred at r.t. for 4 h. The mixture was quenched with $NaHCO_3$, extracted with $CHCl_3$ and washed with aq. $NaHCO_3$ and water, dried over Na_2SO_4, and concentrated. The residue was dissolved in dry methanol (MeOH, 4 ml). To the mixture was added powdered sodium methoxide (*ca* 20 mg) and the mixture was stirred at r.t. for 5 min. The mixture was neutralized with *M* HCl and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4, evaporated and purified on a column of silica gel with hexane-EtOAc (5:1) to give (**13**, 908 mg, 91 %); $[\alpha]_D$ = +46.4° (*c* = 1.15, $CHCl_3$). ^1H NMR δ 7.51-6.93 (m, 15H, 3 Ph), 5.21 (brs, H-1), 5.15 (signal corresponding to small amount of β-anomer, d, H-1β), 4.96, 4.59 (ABq, *J* = 11.1 Hz, PhCH_2), 4.76, 4.68 (ABq, *J* = 12.4 Hz, PhCH_2), 4.52 (s, PhCH_2), 4.02-3.83 (m, H-3,4,5), 3.80 (brt, H-2), 3 .51 (dd, $J_{5,6a}$ = 2.0 Hz, J_{gem} = 12.9 Hz, H-6a), 3. 39 (dd, $J_{5,6b}$ = 6.3 Hz, H-6b), 3.06-2.82 (br, OH); ^{13}C NMR for α-anomer δ 138.22, 138.13 (Ph), 128.55-127.64 (Ph), 92.65 (C-1), 79.41, 75.46, 74.70, 71.41 (C-2,3,4,5), 75.19, 72.76, 72.09 (PhCH_2), 51.61 (C-6); β-anomer δ 93.59 (C-1), 51.16 (C-6).
Anal. Calcd. For $C_{27}H_{29}N_3O_5$: C, 68.19; H, 6.15; N, 8.84. Found: C, 68.26; H, 6.18; N, 8.85.

*6-Azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-mannopyranosyl fluoride (14)*
To a solution of **13** (302 mg, 0.64 mmol) in dry CH_2Cl_2 (4 ml) cooled at -30°C was added DAST (0.2 ml, 1.91 mmol). After 10 min of stirring, the mixture was quenched with MeOH and pored into cold aq. $NaHCO_3$, then extracted with $CHCl_3$ and washed with aq. NaCl, dried over Na_2SO_4, and concentrated *in vacuo*.. The residue was purified on a column of silica gel with hexane-EtOAc (10:1) to give (**14**, 270 mg, 88 %); ^1H NMR δ 7.50-7.10 (m, 15H, 3 Ph), 5.54 (d, 1H, $J_{H,F}$ = 50.2 Hz, H-1), 4.98, 4.62 (ABq, *J* = 11.2 Hz, PhCH_2), 4.81, 4.68 (ABq, *J* = 12.2 Hz, PhCH_2), 4.68, 4.63 (ABq, *J* = 11.9 Hz, PhCH_2), 4.06-3.80 (m, 4H, H-2,3,4,5), 3.56 (dd, $J_{5,6a}$ = 2.0 Hz, J_{gem} = 13.2 Hz, H-6a), 3.41 (dd, $J_{5,6b}$ = 5.0 Hz, H-6b); ^{13}C NMR δ 137.95, 137.68 (Ph), 128.52-127.73 (Ph), 106.13 ($J_{C,F}$ = 223 Hz, C-1), 78.99, 75.35, 74.34, 73.67, 73.55, 73.39, 73.04, 72.49 (C-2,3,4,5,PhCH_2), 51.09 (C-6).

*Methyl 2,4,6-tri-*O*-benzyl-3-*O*-methoxylarbonylmethyl-α-D-galacto-pyranoside (16)*
A solution of the allyl ether **15** (8.03 g, 16 mmol) in dry MeOH (240 ml) was cooled at -78°C and bubbled with O_3. After 30 min, the mixture was quenched with Me_2S and warmed up to r.t. and concentrated *in vacuo*.. The residue was dissolved in 90% aq. MeOH (32 ml). To the mixture was added $NaHCO_3$ (27 g, 0.32 mol) and 2 M Br_2 (in 90% aq. MeOH, 24 ml) was added dropwise with stirring at r.t., and the stirring was continued for 14 h. The reaction mixture was diluted with water and extracted with $CHCl_3$, dried over Na_2SO_4, and evaporated,

purified on a column of silica gel with hexane-EtOAc (3:1) to give **16** (6.61 g, 77 %); $[\alpha]_D$ = +19.7 ° (*c* = 1.45, $CHCl_3$); ^1H NMR δ 7.50-7.19 (m, 15H, 3 Ph), 4.98, 4.65 (ABq, *J* = 11.6 Hz, PhCH_2), 4.76, 4.64 (ABq, *J* = 12.2 Hz, PhCH_2), 4.66 (d, $J_{1,2}$ = 3.6 Hz, H-1), 4.47, 4.36 (ABq, *J* = 11.9 Hz, PhCH_2), 4.14 (d, $J_{3,4}$ = 3.0 Hz, H-4), 4.01 (dd, $J_{2,3}$ = 9.9 Hz, H-2), 3.88 (t, H-5), 3.80 (dd, H-3), 3.73 (s, 3H, OMe), 3.51 (dd, $J_{5,6a}$ = 6.6 Hz, J_{gem} = 9.6 Hz, H-6a), 3. 40 (dd, $J_{5,6b}$ = 5.9 Hz, H-6b), 3.34 (s, 3H, OMe); ^{13}C NMR δ 171.62 (C=O), 138.72, 138.27, 138.04 (Ph), 128.50-127.55 (Ph), 98.24 (C-1), 79.87, 77.39, 75.96, 69.38 (C-2,3,4,5), 74.72, 73.40, 73.21 (PhCH_2), 69.50, 69.33 (C-6, OCH_2), 55.27, 51.70 (OMe).

Anal. Calcd. For $C_{31}H_{36}O_8$: C, 68.39; H, 6.76. Found: C, 68.68; H, 6.75.

*2,4,6-tri-*O*-benzyl-3-*O*-methoxycarbonylmethyl-D-galactopyranose (17)*

Compound **16** (1.88 g, 3.35 mmol) was converted into **17** (875 mg, 50 % 2 steps) by acetolysis followed by de-*O*-acetylation as described for the preparation of **13**.

^1H NMR for the 1-*O*-acetyl intermediate: δ 7.45-7.06 (m, 15H, 3 Ph), 6.38 (d, $J_{1,2}$ = 3.6 Hz, H-1α), 5.54 (d, $J_{1,2}$ = 7.96 Hz, H-1β), 4.98, 4.63 (ABq, *J* = 11.5 Hz, PhCH_2α), 4.68, 4.60 (ABq, *J* = 11.2 Hz, PhCH_2α), 4.45, 4.36 (ABq, *J* = 11.9 Hz, PhCH_2α), 4.43, 4.34 (ABq, *J* = 16.8 Hz, OCH_2α), 4.21 (d, H-4α), 4.13 (dd, $J_{2,3}$ = 10.0 Hz, H-2α), 4.03 (t, H-5), 3.95 (dd, $J_{2,3}$ = 9.6 Hz, H-2β), 3.76 (dd, $J_{3,4}$ = 3.0 Hz, H-3α), 3.73 (s, OMeα), 3.72 (s, OMeβ), 3.51 (dd, $J_{5,6a}$ = 6.9 Hz, J_{gem} = 11.2 Hz, H-6aα), 3. 47 (dd, $J_{5,6b}$ = 5.6 Hz, H-6bα), 2.09 (s, OAc), 2.03 (s, OAc).

Physical data for compound **17**: $[\alpha]_D$ = +0.42° (*c* = 0.7, $CHCl_3$); ^1H NMR δ 7.42-7.02 (m, 15H, 3 Ph), 5.27 (brt, H-1α), 4.96, 4.66 (ABq, *J* = 11.9 Hz, PhCH_2β), 4.95, 4.65 (ABq, *J* = 11.5 Hz, PhCH_2α), 4.76, 4.68 (ABq, *J* = 11.7 Hz, PhCH_2α), 4.62 (d, $J_{1,2}$ = 7.6 Hz, H-1β), 4.47, 4.38 (ABq, *J* = 11.6 Hz, PhCH_2α), 4.41, 4.34 (ABq, *J* = 16.8 Hz, OCH_2α), 4.38, 4.32 (ABq, *J* = 16.8 Hz, OCH_2α), 4.15 (t, H-5α), 4.13 (d, H-4α), 4.07 (d, $J_{3,4}$ = 3.0 Hz, H-4β), 4.02 (dd, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 9.7 Hz, H-2α), 3.80 (dd, $J_{3,4}$ = 3.0 Hz, H-3α), 3.78-3.70 (m, H-2β), 3.74 (s, OMeα), 3.72 (s, OMeβ), 3 .52 (dd, $J_{5,6a}$ = 6.8 Hz, J_{gem} = 9.9 Hz, H-6aα), 3.44 (dd, $J_{2,3}$ = 9.6 Hz, H-3β), 3.42-3.32 (m, H-6bα), 3.16-3.10 (m, OHβ), 2.85 (brs, OHα); ^{13}C NMR δ 171.44 (C=O), 138.60, 138.08, 137.84, 137.75 (Ph), 128.52-127.60 (Ph), 97.77 (C-1β), 97.46 (C-1α), 83.31 (C-3β), 81.22 (C-2β), 79.75 (C-3α), 77.27 (C-2α), 75.65 (C-4α), 74.88, 74.63, 74.52, 73.48, 73.40, 73.04 (PhCH_2), 74.63 (C-4β), 73.75 (C-5β), 69.58 (C-5α), 69.42, 69.34, 69.29, 69.18 (C-6, OCH_2), 51.72 (OMe).

Anal. Calcd. For $C_{30}H_{34}O_8$: C, 68.95; H, 6.56. Found: C, 68.79; H, 6.58.

*Trimethylsilyl 2,4,6-tri-*O*-benzyl-3-*O*-methoxylcarbonylmethyl-β-D-galactopyranoside (18)*

To a stirred solution of **17** (987 mg, 1.89 mmol) in dry toluene (1 ml) was added *N*-(trimethylsilyl)-diethylamine (2 ml), and the mixture was evaporated at 40°C. If the reaction did not proceed completely, the same amount of toluene and reagent was added and concentrated again. The residue was purified on a column of silica gel with hexane-EtOAc (10:1) to give **18** (815 mg, 73 %); $[\alpha]_D$ = -23.6 ° (*c* = 1.2, $CHCl_3$). ^1H NMR δ 7.49-7.11 (m, 15H, 3 Ph), 4.96, 4.68 (ABq, *J* = 11.2 Hz, PhCH_2), 4.92, 4.72 (ABq, *J* = 10.6 Hz, PhCH_2), 4.57 (d, $J_{1,2}$ = 7.3 Hz, H-1), 4.43, 4.36 (ABq, *J* = 11.9 Hz, PhCH_2), 4.38, 4.31 (ABq, *J* = 16.8 Hz, OCH_2), 4.06 (d, $J_{3,4}$ = 3.0 Hz, H-4), 3.75 (dd, $J_{2,3}$ = 9.9 Hz, H-2), 3.71 (s, OMe), 3.58-3.41 (m, 2H, H-5,6a,b), 3.40 (dd, H-3), 0.18 (s, 9H, $SiMe_3$); ^{13}C NMR δ 171.43 (C=O), 138.83, 138.69, 138.08 (Ph), 128.46-127.42 (Ph), 98.22 (C-1), 83.27 (C-3), 81.74 (C-2), 74.90, 74.43, 73.42 (PhCH_2), 74.90, 73.75 (C-4,5), 69.44, 69.31 (C-6, OCH_2), 51.65 (OMe), 0.24 (SiMe).

Anal. Calcd. For $C_{33}H_{42}O_8$: C, 66.64; H, 7.12. Found: C, 66.77; H, 7.22.

2,4,6-tri-O-benzyl-3-O-methoxycarbonylmethyl-β-D-galactopyranosyl-(1-1)-6-azido-2,3,4-tri-O-benzyl-6-deoxy-α-D-mannopyranoside (19)

A mixture of Cp_2HfCl_2 (206 mg, 0.54 mmol, 1.2 equiv.), silver perchlorate ($AgClO_4$) (225 mg, 1.09 mmol, 2.4 equiv.) in dry CH_2Cl_2 (3 ml) was stirred at r.t. for 10 min and cooled to -78 °C. Silylated galactoside (**18**, 269 mg, 0.45 mmol) and mannosyl fluoride **14** (277 mg, 0.58 mmol, 1.3 equiv.) in dry CH_2Cl_2 (6 ml) was added to this mixture and the reaction mixture was stirred for 2 h under Ar at the same temperature and then for 1 h at -70~-50 °C. The reaction was quenched by adding Et_3N at -50 °C and the mixture was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed with aqueous sodium bicarbonate and satuld. NaCl and dried over Na_2SO_4, then evaporated. The residue was subjected to column chromatography on silica gel eluted with hexane-EtOAc (3:1) to give the β-isomer **19** {243 mg, 55 %, m.p. 59-61°C; $[\alpha]_D$ = +18.1° (*c* = 0.9, $CHCl_3$); ^1H NMR δ 7.46-7.0 (m, 30H, 6 Ph), 5.05 (d, $J_{1,2}$ = 1.3 Hz, H-1), 4.95 (ABq, 1H, *J* = 11.2 Hz, PhCH_2), 4.93, 4.68 (ABq, *J* = 11.9 Hz, PhCH_2), 4.69-4.48 (m, 7H, PhCH_2), 4.43 (d, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.37 (s, 2H, PhCH_2), 4.30, 4.22 (ABq, *J* = 16.8 Hz, OCH_2), 4.18-4.11 (m, 1H, H-5), 4.07 (d, $J_{3',4'}$ = 3.0 Hz, H-4'), 3.93 (dd, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 9.7 Hz, H-3), 3.87 (t, H-4), 3.73 (dd, $J_{2',3'}$ = 9.6 Hz, H-2'), 3.71 (s, OMe), 3.60 (t, H-2), 3 .63-3.40 (m, 3H, H-5', 6'a,b), 3.40 (dd, H-3'), 3.30 (d, 2H, $J_{5,6}$ = 4.0 Hz, H-6); ^{13}C NMR δ 171.12 (C=O), 138.58, 138.54, 138.40, 138.34, 138.08, 137.82 (Ph), 128.55-127.60 (Ph), 102.91 ($J_{C',H'}$ = 158.7, C-1'), 99.55 ($J_{C,H}$ = 171.5, C-1), 83.49 (C-3'), 79.80 (C-2'), 79.48 (C-3), 75.27 (C-4), 74.95, 74.61, 73.37, 72.52 (PhCH_2), 74.61 (C-2), 74.07 (C-4'), 73.73 (C-5'), 72.13 (C-5), 69.09 (OCH_2), 68.55 (C-6'), 51.75 (OMe), 51.00 (C-6); Anal. Calcd. For $C_{57}H_{61}N_3O_{12}$: C, 69.85; H, 6.27; N, 4.29. Found: C, 69.53; H, 6.38; N, 4.22.} with a small amount of α-isomer (2,4,6-tri-*O*-benzyl-3-*O*-methoxycarbonylmethyl-α-D-galactopyranosyl-(1-1)-6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-mannopyranoside {**20**, 18 mg, 4.1 %, $[\alpha]_D$ = +51.9 ° (*c* = 1.03, $CHCl_3$); ^1H NMR δ 7.48-7.05 (m, 30H, 6 Ph), 5.23 (d, $J_{1',2'}$ = 3.6 Hz, H-1'), 5.15 (d, $J_{1,2}$ = 1.3 Hz, H-1), 4.96, 4.63 (ABq, *J* = 11.5 Hz, PhCH_2), 4.93, 4.56 (ABq, *J* = 11.2 Hz, PhCH_2), 4.70, 4.64 (ABq, *J* = 11.7 Hz, PhCH_2), 4.60, 4.53 (ABq, *J* = 11.4 Hz, PhCH_2), 4.59 (s, 2H, PhCH_2), 4.45, 4.36 (ABq, *J* = 11.7 Hz, PhCH_2), 4.40, 4.31 (ABq, *J* = 16.8 Hz, OCH_2), 4.11 (d, $J_{3',4'}$ = 2.6 Hz, H-4'), 4.02 (d, $J_{2',3'}$ = 9.9 Hz, H-2'), 4.01-3.90 (m, 1H, H-5), 3.90-3.82 (m, 1H, H-3), 3.88 (t, *J* = 8.9 Hz, H-4), 3.73 (s, OMe), 3.68 (t, H-5'), 3.60 (dd, H-3'), 3.58 (brd, H-2), 3.46-3.35 (m, 2H, H-6'a,b), 3.29 (d, 2H, $J_{5,6}$ = 4.0 Hz, H-6); ^{13}C NMR δ 172.07 (C=O), 139.06, 138.78, 138.69, 138.54, 138.38 (Ph), 128.86-127.96 (Ph), 94.09 ($J_{C,H}$ = 169.7, C-1), 93.93 ($J_{C',H'}$ = 170.0, C-1'), 80.34 (C-3'), 79.37 (C-3), 76.73 (C-2'), 76.06 (C-4'), 75.78 (C-4), 75.63, 75.20, 74.03, 73.03, 72.69, 72.52 (PhCH_2), 74.93 (C-2), 72.45 (C-5), 70.74 (C-5'), 69.85 (OCH_2), 69.67 (C-6'), 52.16 (OMe), 51.79 (C-6); Anal. Calcd. For $C_{57}H_{61}N_3O_{12}$: C, 69.85; H, 6.27; N, 4.29. Found: C, 69.42; H, 6.27; N, 4.29.}.

2,4,6-tri-O-benzyl-3-O-methoxycarbonylmethyl-β-D-galactopyranosyl-(1-1)-6-amino-2,3,4-tri-O-benzyl-6-deoxy-α-D-mannopyranoside (21)

Azide **20** (109 mg, 11.2 mmol) was dissolved in dry MeOH (5 ml) and treated with triphenylphosphine (62 mg, 0.24 mmol). After stirring at r.t. over night, the reaction mixture was concentrated *in vacuo* to dryness. The residue was purified on a column of silica gel with $CHCl_3$-MeOH (20:1) to give **21** (101 mg, 94 %); $[\alpha]_D$ = +5.29° (*c* = 1.0, $CHCl_3$); ^1H NMR δ 7.43-7.06 (m, 30H, 6 Ph), 5.06 (d, $J_{1,2}$ = 1.3 Hz, H-1), 4.93 (ABq, 1H, *J* = 10.9 Hz, PhCH_2), 4.92, 4.66 (ABq, *J* = 11.9 Hz, PhCH_2), 4.64, 4.53 (ABq, *J* = 11.5 Hz, PhCH_2), 4.62, 4.56 (ABq, *J* = 12.2 Hz, PhCH_2), 4.59 (s, 2H, PhCH_2), 4.49 (d, $J_{1',2'}$ = 6.9 Hz, H-1'), 4.36 (s, 2H, PhCH_2), 4.32, 4.24 (ABq, *J* = 16.5 Hz, OCH_2), 4.00-3.90 (m, 1H, H-5), 3.99 (d, $J_{3',4'}$ = 3.0 Hz, H-4'), 3.94 (d, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 3.73 (dd, $J_{2',3'}$ = 9.9 Hz, H-2'), 3.70 (t, H-4), 3.71 (s, OMe), 3.63 (t, H-2), 3 .62-3.55 (m, 1H,

H-5'), 3.50 (dd, $J_{5',6a'}$ = 6.9 Hz, J_{gem} = 9.2 Hz, H-6'a), 3.40 (dd, H-3'), 3.21 (dd, $J_{5',6b'}$ = 4.3 Hz, H-6'b), 2.90 (dd, $J_{5,6a}$ = 2.5 Hz, J_{gem} = 13.5 Hz, H-6a), 2.68 (dd, $J_{5,6b}$ = 8.1 Hz, H-6b); ^{13}C NMR δ 171.25 (C=O), 138.59, 138.43, 138.40, 138.11, 137.34, 132.18, 132.04, 131.97 (Ph), 128.71-127.62 (Ph), 102.66 (C-1'), 99.60 (C-1), 83.49 (C-3'), 79.93, 79.84, 77.23, 76.24, 75.09, 74.39, 73.87, 73.0 (C-2,3,4,5,2',3',4',5'), 74.97, 74.48, 73.44, 72.70, 72.56 (Ph*C*H$_2$), 69.51, 69.36 (OCH$_2$, C-6'), 51.75 (OMe), 42.93 (C-6).
Anal. Calcd. For $C_{57}H_{63}NO_{12}$: C, 71.75; H, 6.66; N, 1.47. Found: C, 61.53; H, 6.72; N, 1.32.

*2,4,6-Tri-*O*-benzyl-3-*O*-methoxycarbonylmethyl-β-D-galactopyranosyl-(1-1)-2,3,4-tri-*O*-benzyl-6-deoxy-6-*N*-dodecanoylamido-α-D-mannopyranoside (22)*

To a solution of **21** (58 mg, 0.061 mmol) dissolved in CH_2Cl_2 (2.5 ml) was added Laulic acid (13 mg, 0.067 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide HCl (WSCI, 13 mg, 0.067 mmol). The mixture was stirred for 3 h at r.t., and diluted with $CHCl_3$, washed with water and satuld. NaCl, dried over Na_2SO_4, and evaporated. The residue was subjected to column chromatography on silica gel eluted with hexane-EtOAc (3:1) to give **22** (61 mg, 88%); ^{1}H NMR δ 7.45-6.98 (m, 30H, 6 Ph), 6.01 (d, 1H, J = 6.6 Hz, NH), 5.02 (d, $J_{1,2}$ = 1.7 Hz, H-1), 4.92 (ABq, 1H, J = 11.9 Hz, PhC*H*$_2$), 4.90 (ABq, 1H, J = 10.6 Hz, PhC*H*$_2$), 4.72-4.47 (m , 8H, PhC*H*$_2$), 4.40 (d, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.38, 4.33 (ABq, J = 11.9 Hz, PhC*H*$_2$), 4.33, 4.25 (ABq, J = 16.8 Hz, OCH$_2$), 4.12-4.03 (m, 1H, H-5), 4.02 (d, $J_{3',4'}$ = 2.6 Hz, H-4'), 3.95 (dd, $J_{2,3}$ = 3.1 Hz, $J_{3,4}$ = 9.4 Hz, H-3), 3.89 (ddd, $J_{5,6a}$ = 7.9 Hz, J_{gem} = 13.9 Hz, H-6a), 3.74 (dd, $J_{2',3'}$ = 9.9 Hz, H-2'), 3.73 (t, H-4), 3.71 (s, OMe), 3.61 (t, H-2), 3.57-3.46 (m, 2H, H-5'6'a), 3.39 (dd, H-3'), 3.30-3.21 (m, 1H, H-6'b), 3.14 (dt, H-6b), 2.03 (t, J = 7.4 Hz, COCH$_2$), 1.65-1.40 (m, 2H, COCH$_2$C*H*$_2$), 1.24 (brs, 16H, CH$_2$), 0.87 (t, J = 6.8 Hz, CH$_3$).

*3-*O*-(Carboxymethyl)-β-D-galactopyranosyl-(1-1)-6-deoxy-6-*N*-dodecanoylamido-α-D-mannopyranoside (3)*

22 (56 mg, 0.04 mmol) was dissolved in MeOH (2 ml) and $CHCl_3$ (1 ml), and 20 % Pd(OH)$_2$ on carbon (~20 mg) was added to the mixture. To the reaction was stirred under hydrogen atmosphere. After the reaction was complete (~4 h), the mixture was filtered and concentrated *in vacuo*, then dissolved in 0.25 *N* NaOH (0.5 ml). After 30 min, the reaction mixture was neutralized with 50 % acetic acid, purified by Bio Gel P-2 column chromatography (eluted with H_2O), and lyophilized to give **3** (14 mg, 73 %: 2 steps); $[\alpha]_D$ = +35.3° (*c* = 0.23, MeOH-H_2O = 1:1). ^{1}H NMR (400 MHz) δ 5.16 (s, H-1), 4.62 (d, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.14 (s, 3H, H-4', OCH$_2$), 4.09 (brs, 1H, H-2), 4.04-3.95 (m, 1H, H-5), 3.90 (dd, $J_{2,3}$ = 3.4 Hz, $J_{3,4}$ = 9.8 Hz, H-3), 3.80 (br, 2H, H-6a'b'), 3.77-3.61 (m, 3H, H-6a, 2', 5'), 3.62 (t, H-4), 3.54 (br, 1H, H-3'), 3.45 (br, 1H, H-6'b), 2.31 (t, J = 7.4 Hz, COCH$_2$), 1.69-1.55 (m, 2H, COCH$_2$CH$_2$), 1.31 (brs, 16H, CH$_2$), 0.89 (t, J = 6.8 Hz, CH$_3$); ^{13}C NMR (400 MHz) δ 103.04 (C-1'), 102.07 (C-1), 82.65 (C-3'), 76.01 (C-2'), 72.37 (C-5), 70.82, 70.71 (C-3,5'), 70.49 (C-2), 69.34 (C-4'), 68.75 (C-4), 66.17 (OCH$_2$), 61.81 (C-6'), 40.84 (C-6), 36.68 (COCH$_2$), 34.41, 33.82, 32.45, 30.10, 30.05, 30.00, 29.85, 29.80, 29.74, 29.65, 26.48, 23.20, 14.52 (CH$_3$). FAB MS m/z: 580 [M-H]$^-$.

*2,4,6-Tri-*O*-benzyl-3-*O*-methoxycarbonylmethyl-β-D-galactopyranosyl-(1-1)-2,3,4-tri-*O*-benzyl-6-deoxy-6-*N*-(11-carboxyundecanoylamido)-α-D-mannopyranoside (23) and 1,10-bis[2,4,6-tri-*O*-benzyl-3-*O*-methoxycarbonylmethyl-β-D-galactopyranosyl-(1-1)-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-mannopyranoside-6-yl]-dicarboxyamidedecane (28)*

Compound **21** (43 mg) was treated with 1,10-decandicarboxylic acid (11 mg) and WSCI (9.5 mg) in CH_2Cl_2 (2 ml) as described for the synthesis of **22** to yield **23** (8 mg, 15%) and **28** (47 mg, 83%).

NMR data for **23**; ^{1}H NMR δ 7.42-7.09 (m, 30H, 6 Ph), 6.12 (d, 1H, J = 7.3 Hz, NH), 5.02 (brs, H-1), 4.91 (ABq, 1H, J = 11.9 Hz, PhCH_2), 4.90 (ABq, 1H, J = 10.6 Hz, PhCH_2), 4.70-4.57 (m , 6H, PhCH_2), 4.53 (ABq, 1H, J = 11.6 Hz, PhCH_2), 4.52 (ABq, 1H, J = 12.5 Hz, PhCH_2), 4.39 (d, $J_{1',2'}$ = 7.6 Hz, H-1'), 4.38, 4.33 (ABq, PhCH_2), 4.33, 4.25 (ABq, J = 16.8 Hz, OCH$_2$), 4.07 (ddd, 1H, $J_{4,5}$ = 9.6 Hz, $J_{5,6a}$ = 6.3 Hz, $J_{5,6b}$ = 3.3 Hz, H-5), 4.02 (d, $J_{3',4'}$ = 3.0 Hz, H-4'), 3.95 (dd, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 3.98-3.84 (m, 1H, H-6a), 3.78-3.66 (m, 2H, H-4, 2'), 3.71 (s, OMe), 3.60 (brt, H-2), 3.58-3.46 (m, 2H, H-5', 6'a), 3.39 (dd, $J_{2',3'}$ = 9.9 Hz, H-3'), 3.29-3.20 (m, 1H, H-6'b), 3.13 (dt, J_{gem} = 13.5 Hz, H-6b), 2.30 (t, J = 7.6 Hz, CH_2COOH), 2.04 (t, J = 7.6 Hz, COCH$_2$), 1.68-1.45 (m, 4H, COCH$_2$CH_2, CH_2CH$_2$COOH), 1.23 (brs, 12H, CH$_2$); ^{13}C NMR δ 177, 173.60, 171.34 (C=O), 138.57, 138.42, 138.34, 138.08, 137.18 (Ph), 128.70-127.65 (Ph), 102.51 (C-1'), 99.33 (C-1), 83.43 (C-3'), 79.87, 79.57, 76.10, 75.29, 75.00, 74.48, 74.30, 73.94, 73.57, 72.65, 70.85, 69.65, 69.29, 51.79 (OMe), 39.87, 36.31, 33.89, 29.27, 29.09, 28.93, 28.79, 25.75, 24.64.

^{1}H NMR data for **28**; δ 7.41-7.08 (m, 60H, 12 Ph), 6.00 (d, 2H, J = 6.6 Hz, NH), 5.02 (brs, H-1), 4.91 (ABq, 2H, J = 11.9 Hz, PhCH_2), 4.89 (ABq, 2H, J = 10.6 Hz, PhCH_2), 4.71-4.56 (m , 12H, PhCH_2), 4.53 (ABq, 2H, J = 11.6 Hz, PhCH_2), 4.51 (ABq, 2H, J = 12.5 Hz, PhCH_2), 4.39 (d, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.38, 4.33 (ABq, PhCH_2), 4.33, 4.25 (ABq, J = 16.8 Hz, OCH$_2$), 4.11-4.03 (m, 2H, H-5), 4.02 (d, $J_{3',4'}$ = 3.0 Hz, H-4'), 3.95 (dd, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.96-3.83 (m, 2H, H-6a), 3.79-3.66 (m, 4H, H-4, 2'), 3.71 (s, OMe), 3.60 (brt, H-2), 3.58-3.45 (m, 4H, H-5', 6'a), 3.38 (dd, $J_{2',3'}$ = 9.6 Hz, H-3'), 3.32-3.29 (m, 2H, H-6'b), 3.14 (dt, J_{gem} = 13.5 Hz, H-6b), 2.02 (t, J = 7.0 Hz, COCH$_2$), 1.62-1.41 (m, 4H, COCH$_2$CH$_2$), 1.21 (brs, 12H, CH$_2$).

*3-O-(Carboxymethyl)-β-D-galactopyranosyl-(1-1)-6-deoxy-6-*N*-(11-carboxyundecanoylamido)-α-D-mannopyranoside (4)*

Compound **23** (19 mg) was deprotected as described for the synthesis of **3** to give **4** (11 mg, 90 %: 2 step); $[\alpha]_D$ = +38.5° (c = 0.12, MeOH-H$_2$O = 1:1). ^{1}H NMR (400 MHz) δ 5.16 (d, $J_{1,2}$ = 1.7 Hz, H-1), 4.62 (d, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.28, 4.23 (ABq, J = 16.5 Hz, OCH$_2$), 4.17 (d, $J_{3',4'}$ = 3.1 Hz, H-4'), 4.09 (dd, $J_{2,3}$ = 3.4 Hz, H-2), 4.00 (ddd, 1H, $J_{4,5}$ = 9.8 Hz, $J_{5,6a}$ = 6.4 Hz, $J_{5,6b}$ = 3.1 Hz, H-5), 3.89 (dd, $J_{3,4}$ = 9.8 Hz, H-3), 3.80 (d, 2H, J = 6.0 Hz, H-6a'b'), 3.73 (dd, $J_{2',3'}$ = 9.8 Hz, H-2'), 3.72 (t, J = 6.4 Hz, H-5'), 3.62 (t, H-4), 3.61 (dd, J_{gem} = 14.5 Hz, H-6a), 3.56 (dd, H-3'), 3.48 (dd, H-6b), 2.40 (t, J =7.5 Hz, CH_2COOH), 2.31 (t, J = 7.5 Hz, COCH$_2$), 1.62 (brt, 4H, COCH$_2$CH_2, CH_2CH$_2$COOH), 1.32 (brs, 14H, CH$_2$); ^{13}C NMR (400 MHz) δ 178.71, 177.23 (C=O), 102.91 (C-1), 101.89 (C-1'), 82.55(C-3'), 76.09, 72.27, 70.79, 70.69, 70.48, 68.82, 68.24, 66.02, 62.09, 61.72 (C-6'), 40.88 (C-6), 36.60, 34.76, 29.33, 29.28, 29.19, 29.09, 29.01, 26.28, 25.18. FAB MS m/z: 610 [M-H]$^-$, 632 [M+Na-2H]$^-$.

1,10-Bis[3-O-(carboxymethyl)-β-D-galactopyranosyl-(1-1)-6-deoxy-α-D-mannopyranoside-6-yl]-dicarboxylamidedecane (29)

Compound **27** (20 mg) was deprotected as described for the synthesis of **3** to give **29** (19 mg, 93 %: 2 steps); $[\alpha]_D$ = +42.7° (c = 0.2, MeOH-H$_2$O = 1:1). ^{1}H NMR (400 MHz) δ 5.16 (d, $J_{1,2}$ = 1.7 Hz, H-1), 4.63 (d, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.13 (d, $J_{3',4'}$ = 2.8 Hz, H-4'), 4.11 (s, OCH$_2$), 4.09 (dd, $J_{2,3}$ = 3.4 Hz, H-2), 4.00 (ddd, 2H, $J_{4,5}$ = 9.5 Hz, $J_{5,6a}$ = 6.1 Hz, $J_{5,6b}$ = 3.1 Hz, H-5), 3.90 (dd, $J_{3,4}$ = 9.8 Hz, H-3), 3.79 (d, 4H, J = 6.1 Hz, H-6a'b'), 3.72 (brt, H-2'), 3.72 (brt, H-5'), 3.62 (t, H-4), 3.61 (dd, J_{gem} = 14.4 Hz, H-6a), 3.52 (dd, $J_{2',3'}$ = 9.8 Hz, H-3'), 3.47 (dd, H-6b), 2.31 (t, J = 7.5 Hz, COCH$_2$), 1.60 (brt, 4H, COCH$_2$CH_2), 1.32 (brs, 12H, CH$_2$); ^{13}C NMR (400 MHz) δ 178.56 (C=O), 102.94 (C-1'), 101.79 (C-1), 82.65 (C-3'), 76.01, 72.19, 70.71, 70.53,

70.41, 68.68, 65.92, 61.69 (C-6'), 40.76 (C-6), 36.53 ($COCH_2$), 29.31, 29.16, 29.09, 26.23. FABMS m/z: 991 $[M-H]^-$, 1013 $[M+Na-2H]^-$.

2,4,6-Tri-O-benzyl-3-O-methoxycarbonylmethyl-β-D-galactopyranosyl-(1-1)-2,3,4-tri-O-benzyl-6-deoxy-6-N-(12-tert-butoxycarbonylamido-undecanoylamido)-α-D-mannopyranoside (24)

Compound **21** (78 mg) was treated with *tert*-butoxycarbonylundecanoic acid (28 mg) and WSCI (17 mg) in CH_2Cl_2 (3 ml) as described for the synthesis of **22** to yield **24** (90 mg, 90 %). ^1H NMR δ 7.44-7.05 (m, 30H, 6 Ph), 6.00 (d, 1H, J = 6.6 Hz, NHCO), 5.02 (d, $J_{1,2}$ = 2.0 Hz, H-1), 4.91 (ABq, 1H, J = 11.6 Hz, PhCH_2), 4.90 (ABq, 1H, J = 10.6 Hz, PhCH_2), 4.71-4.44 (m , 8H, PhCH_2), 4.40 (d, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.38, 4.33 (ABq, PhCH_2), 4.33, 4.25 (ABq, J = 16.8 Hz, OCH_2), 4.13-4.02 (m, 1H, H-5), 4.02 (d, $J_{3',4'}$ = 3.0 Hz, H-4'), 3.95 (dd, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 3.99-3.83 (m, 1H, H-6a), 3.78-3.77 (m, 2H, H-4, 2'), 3.72 (s, OMe), 3.61 (dd, H-2), 3.56-3.45 (m, 2H, H-5', 6'a), 3.39 (dd, $J_{2',3'}$ = 3.0 Hz, H-3'), 3.32-3.21 (m, 1H, H-6'b), 3.14 (dt, J_{gem} = 13.9 Hz, H-6b), 3.14-3.02 (m, 2H, CH_2NH), 2.04 (t, J = 7.4 Hz, $COCH_2$), 1.60-1.35 (m, 12H, $COCH_2CH_2$, $BocCH_3$), 1.23 (brs, 16H, CH_2), 0.87 (t, J = 6.8 Hz, CH_3).

3-O-(Carboxymethyl)-β-D-galactopyranosyl-(1-1)-6-deoxy-6-N-(12-amino-undecanoylamido)-α-D-mannopyranoside (5)

Compound **24** (90 mg) was at first treated with $Pd(OH)_2$ (~20 mg)-H_2 followed by saponification as described for the synthesis of **3** to give tBoc-protected intermediate, which was finally treated with TFA (1 ml) in MeOH (1 ml) at 0 °C for 10 min and concentrated with Speed Vac under high vacuum. The resulting material was dissolved in water (0.5 ml) which was basified with 1*N* NaOH then neutralized with 50% AcOH. The mixture was purified on a column of Biogel P-2 to give **5** (33 mg, 77 %: 3 steps); $[\alpha]_D$ = +32.3° (c = 0.2, MeOH-H_2O = 1:1). ^1H NMR (400 MHz) δ 5.16 (d, $J_{1,2}$ = 1.5 Hz, H-1), 4.62 (d, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.12 (d, $J_{3',4'}$ = 2.9 Hz, H-4', 4.10 (s, 2H, OCH_2), 4.09 (dd, $J_{2,3}$ = 3.4 Hz, H-2), 4.00 (ddd, 1H, $J_{4,5}$ = 10.2 Hz, $J_{5,6a}$ = 6.7 Hz, $J_{5,6b}$ = 3.2 Hz, H-5), 3.90 (dd, $J_{3,4}$ = 9.8 Hz, H-3), 3.80 (d, 2H, J = 6.4 Hz, H-6a'b'), 3.72 (dd, $J_{2',3'}$ = 9.8 Hz, H-2'), 3.61 (t, H-4), 3.60 (dd, J_{gem} = 15.1 Hz, H-6a), 3.50 (dd, H-3'), 3.49 (dd, H-6b), 3.00 (t, J = 7.6 Hz, CH_2NH_2), 2.31 (t, J = 7.3 Hz, $COCH_2$), 1.71-1.54 (m, 2H, $COCH_2CH_2$), 1.32 (brs, 16H, CH_2); ^{13}C NMR (400 MHz) δ 179.24, 178.66 (C=O), 102.88 (C-1'), 101.71 (C-1), 82.82 (C-3'), 76.17 (C-5'), 72.20 (C-5), 70.77 (C-3), 70.58 (C-2'), 70.49 (C-2), 69.26 (OCH_2), 69.00 (C-4), 66.02 (C-4'), 61.82 (C-6'), 41.01 (C-6), 40.38 (CH_2NH_2), 36.61 ($COCH_2$), 29.42, 29.39, 29.29, 29.24, 29.00, 27.53, 26.38, 26.28. FABMS m/z: 595 $[M-H]^-$

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2,4,6-Tri-O-benzyl-3-O-methoxycarbonylmethyl-β-D-galactopyranosyl-(1,1)-2,3,4-tri-O-benzyl-6-deoxy-6-N-(6-hydroxyhexanoylamido)-α-D-mannopyranoside (26)

Compound **21** (74 mg) was treated with 6-trityloxyhexanolic acid (32 mg) and WSCI (16 mg) in CH_2Cl_2 (2 ml) as described for the synthesis of **22** to yield **25**, which was dissolved in 80 % AcOH (1 ml) and heated at 70°C for 1h. The mixture was concentrated *in vacuo* and coevaporated with toluene. The resulting residue was purified on a column of silica gel eluted with hexane-EtOAc (1:10) to afford **26** (50.2 mg, 82 %). ^1H NMR δ 7.48-7.00 (m, 30H, 6 Ph), 6.14 (d, 1H, J = 6.9 Hz, NH), 5.02 (d,$J_{1,2}$ = 1.3 Hz, H-1), 4.91 (ABq, 1H, J = 11.9 Hz, PhCH_2), 4.91 (ABq, 1H, J = 10.6 Hz, PhCH_2), 4.72-4.46 (m , 8H, PhCH_2), 4.39 (d, $J_{1',2'}$ = 7.6 Hz, H-1'), 4.36 (s, 2H, PhCH_2), 4.33, 4.26 (ABq, J = 16.8 Hz, OCH_2), 4.08 (ddd, 1H, $J_{4,5}$ = 9.6 Hz, $J_{5,6a}$ = 6.3 Hz, $J_{5,6b}$ = 3.3 Hz, H-5), 4.02 (d, $J_{3',4'}$ = 3.0 Hz, H-4'), 3.96 (dd, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 3.99-3.84 (m, 1H, H-6a), 3.74 (dd, $J_{2',3'}$ = 9.9 Hz, H-2'), 3.79-3.66 (m, 1H, H-4), 3.71 (s, OMe), 3.61 (brt, H-2), 3.58-3.46 (m,

4H, H-5', 6'a, C*H*$_2$OH), 3.42 (dd, H-3'), 3.29-3.19 (m, 1H, H-6'b), 3.11 (dt, J_{gem} = 13.2 Hz, H-6b), 2.05 (t, J = 7.3 Hz, COCH$_2$), 1.92-1.75 (br, 1H, OH), 1.70-1.40 (m, 4H, COCH$_2$C*H*$_2$, C*H*$_2$CH$_2$OH), 1.40-1.18 (m, 2H, CH$_2$). ^{13}C NMR δ 173.06, 171.35 (C=O), 138.60, 138.40, 138.34, 138.02, 137.14 (Ph), 128.70-127.55 (Ph), 102.28 (C-1'), 99.21 (C-1), 83.36, 79.86, 79.55, 76.15, 75.26, 75.06, 74.97, 74.46, 74.30, 73.98, 73.57, 72.70, 72.65, 70.82, 69.76, 69.25, 62.46, 51.75, 39.82, 36.30, 32.18, 25.46, 25.35.

*3-O-(Carboxymethyl)β-D-galactopyranosyl-(1-1)-6-deoxy-6-*N*-(6-sulfoxyhexanoylamido)-α-D-mannopyranoside (6)*

To a solution of **26** (50 mg, 0.049 mmol) in DMF (0.5 ml) was added dropwise pyridine sulfurtrioxide complex (39 mg, 0.25 mmol) in DMF (0.5 ml). The mixture was stirred for 0.5 h at r.t. and was neutralized with Dowex 50 (Na) and purified on a column of silica gel eluted with CHCl$_3$-MeOH (10:1) to yield the sulfated **27** (47 mg). The sulfate was then subjected to deprotection as described for the synthesis of **3** to yield **6** (22 mg, 73 % : 3 steps). ^{1}H NMR δ 5.17 (s, H-1), 4.64 (d, $J_{1',2'}$ = 7.6 Hz, H-1'), 4.19-4.05 (m, 6H, H-2, 4', OCH$_2$, CH$_2$OSO$_3$), 4.00 (ddd, 1H, $J_{4,5}$ = 9.5 Hz, $J_{5,6a}$ = 6.1 Hz, $J_{5,6b}$ = 3.1 Hz, H-5), 3.90 (dd, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 9.9 Hz, H-3), 3.79 (d, 2H, J = 6.3 Hz, H-6a'b'), 3.77-3.58 (m, 3H, H-6a, 2', 5'), 3.62 (t, H-4), 3.54 (dd, H-3'), 3.48 (dd, J_{gem} = 14.4 Hz, H-6b), 2.34 (t, J = 7.5 Hz, COCH$_2$), 1.80-1.60 (m, 4H, COCH$_2$C*H*$_2$, C*H*$_2$CH$_2$OSO$_3$), 1.43 (brq, 2H, CH$_2$). FABMS m/z: 592 [M-H]$^-$, 614 [M+Na-2H]$^-$.

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