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Novel Mimics of Sialyl Lewis X: Design, Synthesis and Biological Activity of a Series of 2- and 3-Malonate Substituted Galactoconjugates†

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Abstract—A series of potent inhibitors of P-selectin as potential anti-inflammatory agents is reported. These compounds are derivatives of galactocerebrosides bearing a malonate side chain in positions 2 and 3 of the galactose moiety. Based on the binding mode of sialyl Lewis X, the two acidic groups of the malonate are designed to form ionic interactions with two important lysines in the active site of P-selectin, Lys113 and Lys111. On the other hand, the 4- and 6-hydroxy groups on the galactose ring are arranged to chelate the calcium ion in the P-selectin active site. The synthesis and the biological activity of this series of compounds are described. Lead compounds having a greater potency than sialyl Lewis X are identified.

Introduction

The selectins are a highly conserved gene family having a common structural organization and are implicated in the inflammatory response to tissue injury and infection. The first event in this inflammatory cascade is the attachment of leukocytes to cells of the vascular endothelium proximal to the site of trauma. The selectins support this adhesion by interacting with oligosaccharides of the sialyl Lewis X (**1**, Fig. 1) (sLe^x) family presented by glycoproteins or glycolipids on the surface of leukocytes.[1] As expected for a protein–carbohydrate interaction, the binding of selectins to sLe^x is of low-affinity (0.5–1.0 mM).[2] Therefore, it has been postulated that in order to tether circulating leukocytes in vivo, there must be multivalent interactions between clustered patches of sLe^x and the protein.

P-selectin is found in platelets as well as in endothelial cells activated by thrombin and other mediators. E-selectin is expressed by vascular endothelial cells after stimulation by endotoxins and cytokines associated with infection and inflammation and interact with lymphocytes and neutrophils. L-selectin is present on the surface of most lymphocytes and neutrophils and supports their adhesion to endothelium.[3]

The selectins are transmembrane glycoproteins containing an amino-terminal C-type lectin domain which is believed to be the site of carbohydrate recognition. The epidermal growth factor (EGF) repeat and a variable number of complement regulatory-like repeats constitute the main structural difference between E-, P-, and L-selectins.[1]

On the basis of the homology with mannose binding protein, a C-type lectin whose structural coordinates have been generated by X-ray,[4] models for the lectin domain of E- and P-selectin have been derived. Various point mutants of E- and P-selectins were prepared and allowed the identification of a small groove located at

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the surface of the protein as a potential binding site.[5–7] This pocket is in the vicinity of a calcium cation found in all selectins as well as in the mannose binding protein. An analysis of the critical residues for binding to P- and E-selectin has revealed the importance of the conserved Lys 113 for P-selectin and both conserved Lys 111 and Lys 113 for E-selectin, located in this shallow groove.[5–8] The recently published crystal structure of the lectin and EGF domains of E-selectin has corroborated the previous models and provides useful structural details to elucidate the recognition of sLe^x epitope by the selectins.[9]

The sialyl Lewis X determinant binds to E-, P-, and L-selectins through calcium dependent interactions.[10] Although the role of calcium in ligand interactions has not been unambiguously established, various SARs of sLe^x-containing oligosaccharides[11–15] suggests that the critical fucosyl residue in sLe^x interacts with the protein similarly to the binding of mannose with the mannose binding protein (MBP). The crystal structure of this mannose–MBP complex has revealed that the key feature of this interaction is the direct chelation of calcium ion by the 3- and 4-hydroxyls of mannose.[4]

The analogy of fucose with mannose complexed in the mannose binding protein was used as the starting point to develop a model of the complex sLe^x–selectin. The known solution NMR structures of sLe^x were docked into the ligand binding site of selectins. Interestingly, the calcium–fucose interaction in E- or P-selectin orients the ligand so that the negatively charged group of the sialic acid moiety is in a suitable position for an ionic interaction with Lys 113.[7] From previous binding studies, this carboxylate group of the sialic acid residue was precisely designated as part of the binding domain of sLe^x glycotope along with the galactose residue.[11–15] A schematic representation of these published binding interactions is shown in Figure 2.

In an effort to develop antagonists to the binding of selectins ligands that would be chemically and structurally simpler than sLe^x, the structural requirements previously described for sLe^x binding to selectins were modeled. Several publications[16–18] have recently reported sLe^x mimics that retain diverse degrees of carbohydrate character. Among them, the monosaccharide **2** (TBC-265) (Fig. 3) containing a carboxylic acid attached to a mannose sugar via a biphenyl template was proved to be as potent as sLe^x.[19] Moreover, this compound inhibited neutrophil migration in rat and mouse models of inflammation when administered subcutaneously. It is in light of these results that we report our efforts directed to the identification of novel glycotope inhibitors of P-selectin adhesion. Glycomimetics of sialyl Lewis X were designed and their synthesis and biological affinity to P-selectin are reported in this paper.

Design Considerations

A convergent strategy was used to design the series of malonate derivatives reported here. In a first approach, the minimum structural requirements previously described for sLe^x binding to selectins were patterned. The second structural element used was that of sulfatide (**3**, Fig. 4), which was shown to bind to the P-selectin receptor with an avidity that is equivalent to that of the myeloid HL-60 cell line.[20] In the case of the sulfatides, the negatively charged sulfate group is suspected to make an ionic interaction with Lys 113 and/or Lys 111 in P-selectin as for the carboxylate group of the sialic acid moiety in sLe^x. Moreover, since glycosphingolipids can coaggregate in patches on cell surfaces,[21] this natural mechanism could generate specific recognition as it is presumed for the natural ligand. These known structural features required for binding to selectins were consequently combined in one simpler saccharide motif.

In replacing the fucose ring in sLe^x by the galactose sugar of the sulfatides in which the 4- and 6-hydroxy groups can act as calcium chelators, an additional acidic functionality at position 3 of this galactose ring has to be introduced in order to mimic the carboxylate group of sialic acid in sLe^x or the sulfate group in sulfatides. The new structure should, in theory, interact with the two critical binding features of the selectins, Lys 113 and the calcium ion. The acidic functionality insertion in position 2 of the galactose ring should also be considered since the 4- and 6-hydroxyl groups are still available for a chelation with the calcium ion.

Finally, the presence of another conserved lysine (Lys 111) proximal to Lys 113 (~4–5 Å) in the selectin binding cavity was shown to be as crucial as Lys 113 for the binding of the sulfatides.[7] It is consequently reasonable to consider this residue as an additional binding feature in the active site of the protein. To take advantage of the chemical nature of this additional residue in the binding cavity, the malonate functionality was contemplated. Both acidic groups should interact with Lys

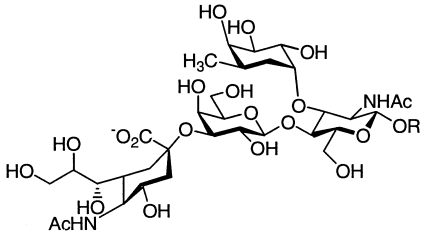


Figure 1. Sialyl Lewis X (**1**).

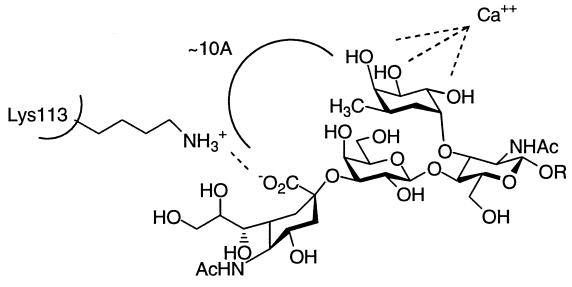


Figure 2. Assumed binding interactions in selectin–sLe^x model.

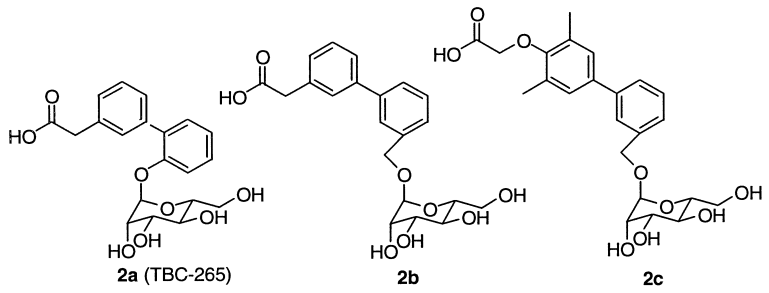


Figure 3. Biphenyl mannoses.

113 and Lys 111. Examples of malonate derived sLe^x mimetics have been reported[22] and have shown, in most cases, slight potency improvements over sLe^x. However, no proof of the binding to the two lysines was established.

This paper describes the preparation of series of malonate derivatives of type I and II (Fig. 5) with the objective of identifying potent P-selectin antagonists. Their SARs, evaluated in P-selectin in vitro models and in the dermal reverse passive Arthus reaction in rats will give insights into the means by which these ligands interact with the protein and would allow validating the previous hypothesis elaborated for their possible binding mode.

Chemistry

The preparation of the different galactosides is outlined in Schemes 1–6. Dimethyl(methylthio)sulfonium triflate promoted glycosidations were used to obtain the different glycolipids as described by Fugedi and Garegg.[23] The key thioglycosides were all prepared from ethyl 1-thio-β-D-galactopyranoside[24] employing the usual protection schemes used in classical carbohydrate chemistry. Most of the final compounds were tested as disodium salts by treatment of the diacids with an aqueous solution of sodium bicarbonate.

2-Substituted galactoconjugates

The preparation of malonate substituted galactolipids in position 2 is described in Schemes 1, 3 and 5. In the aim of excluding any ambiguity in regard to the distance between the two binding features of the molecules, two carbon chain spacers were evaluated ($n=2$ and 4). The protection scheme used to obtain the adequately protected 1-thio-β-galactopyranoside common intermediate **6** (Scheme 1) involves initial formation of the related 3,4-acetonide **5**[25] followed by selective silylation in position 6. The synthesis of the butylmalonyl 1-thio-β-D-galactopyranoside intermediate **18** (Scheme 1) was performed by alkylating the 2-position of 1-thio-galactopyranoside **6**, in presence of sodium hydride, with 1,4-dibromobutane. Subsequent malonic displacement of the remaining bromide functionality in **7** gave the desired compound **8**. In order to study the effect of a 3-blocked position in this series of compounds, intermediate **8** was then submitted to a last protection sequence. Deblocking of the 3, 4 and 6 positions in the galactose sugar by acidic treatment and protection of the 4- and 6-hydroxy groups with benzaldehyde dimethylacetal liberated the 3-position which became available for a benzoylation reaction to give compound **18**.

All attempts to apply the same synthetic scheme for the preparation of the ethylmalonyl analogue **20** appeared to be unsuccessful due to elimination of the alkylating agent. Consequently, the goal was achieved by alkylation of intermediate **6** with *t*-butylbromoacetate to give compound **9**, followed by reduction of the ester group and transformation of the resulting alcohol **10** to a mesylate group. The malonic substitution, catalytically assisted by sodium iodide, was then feasible and the desired ethylmalonyl 1-thio-β-D-galactopyranoside **12** was obtained. Again, as for the 4C analogue, similar protection-deprotection steps were performed and intermediate **20** was available for the next glycosidation reactions.

To produce non-benzoylated galactoconjugates in position 3 such as compounds **33**, **34** (Scheme 3), and **62** (Scheme 5), intermediates **8** ($n=2$) or **12** ($n=4$) were required since removal of all protecting groups could be done in one step. Hence, coupling of D-erythro-azidosphingosine[26] **28** with **8** or **12** under solvent modified Fugedi and Garegg[23] procedure gave galactocerebrosides

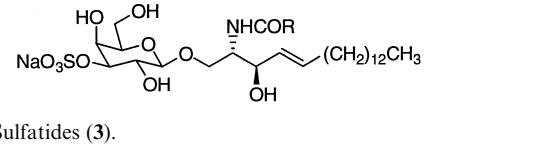


Figure 4. Sulfatides (**3**).

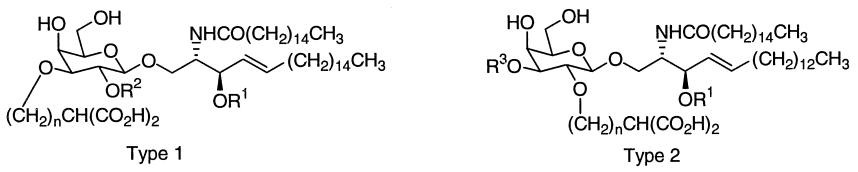
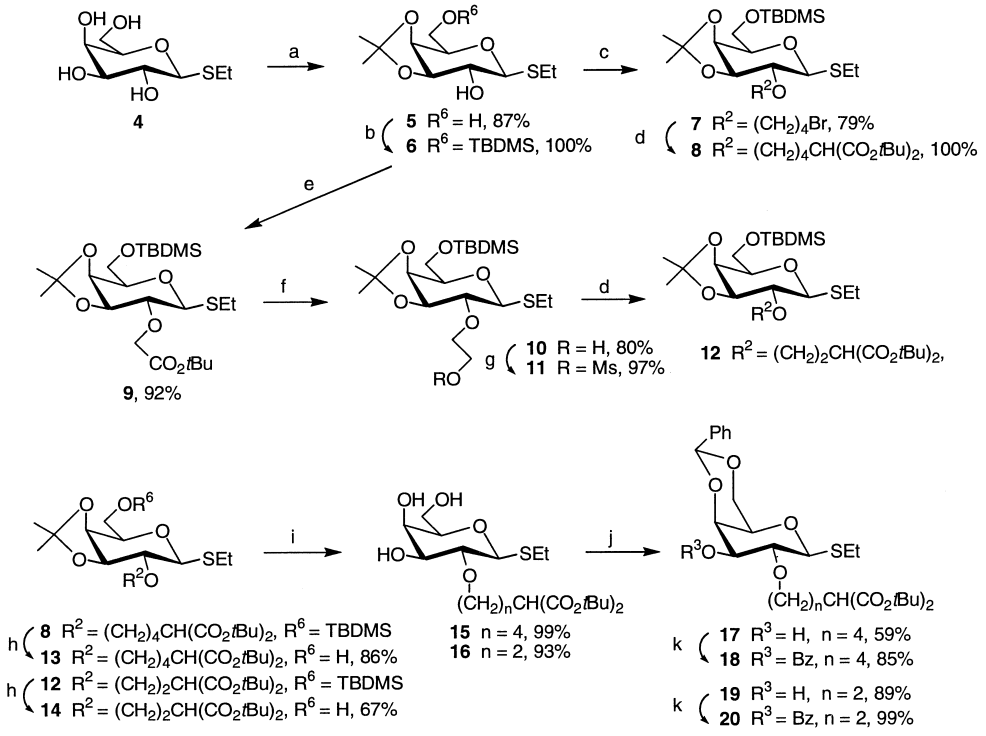


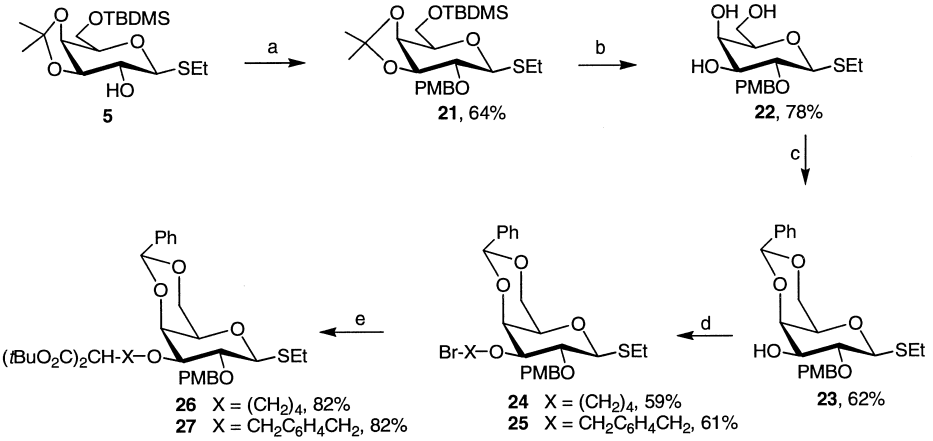
Figure 5. Types of malonate derivatives.

29a and **b** or **31a** and **b**. The choice of solvent appeared to be very peculiar, since silylation of the glycosyl acceptor followed by intramolecular glycosidation by the free 6-hydroxyl group (**35**)[27] under dimethyl(methylthio)sulfonium triflate conditions was an important side reaction. Use of a nonpolar solvent such as toluene or methylene chloride overcomes this problem. The α:β anomers ratio using these solvents varied from 1:1 to 2:1. Each resulting azido-sphingosine anomers were separately reduced and acylated as described by Schmidt et al.[28] prior to trifluoroacetic acid treatment that removed all the protecting groups. Compound **62a** or **b** bearing a methoxycarbonyloctyl side-chain[29] as lipid aglycone were obtained the same way (Scheme 5). The glycosidation reaction afforded in this case a α:β ratio of approximately 1:1.

3-Benzoylated galactolipids **41**, **43** (Scheme 3), and **60** (Scheme 5) were synthesized from glycosides **18** ($n=4$) or **20** ($n=2$) in which the benzoyl group is already in place. Glycosidation with azido-sphingosine[26] followed by separation of the anomers gave galactocerebrosides **36a** and **b** ($n=4$) and **38a** and **b** ($n=2$) in an approximately 7:3 α:β ratio. Usual hydrogen sulfide reduction of the azido functionality and acylation of the resulting amine with palmitoyl chloride afforded intermediates **37a** and **b** ($n=4$) and **39a** and **b** ($n=2$). Two subsequent acidic treatments removed the 4,6-benzylidene protecting



Scheme 1. (a) $CH_3C(OCH_3)_2CH_3$, PTSA; (b) TBDMSCl, pyridine, DMAP; (c) NaH, $Br(CH_2)_4Br$, DMF; (d) $NaCH(CO_2tBu)_2$, THF, DMF; (e) NaH, $BrCH_2CO_2tBu$, DMF; (f) LAH, THF; (g) MsCl, NEt_3, CH_2Cl_2; (h) nBu_4NF, THF; (i) 3 N HCl, THF; (j) $PhCH(OCH_3)_2$, MeCN, PTSA; (k) BzCl, py, DMAP.



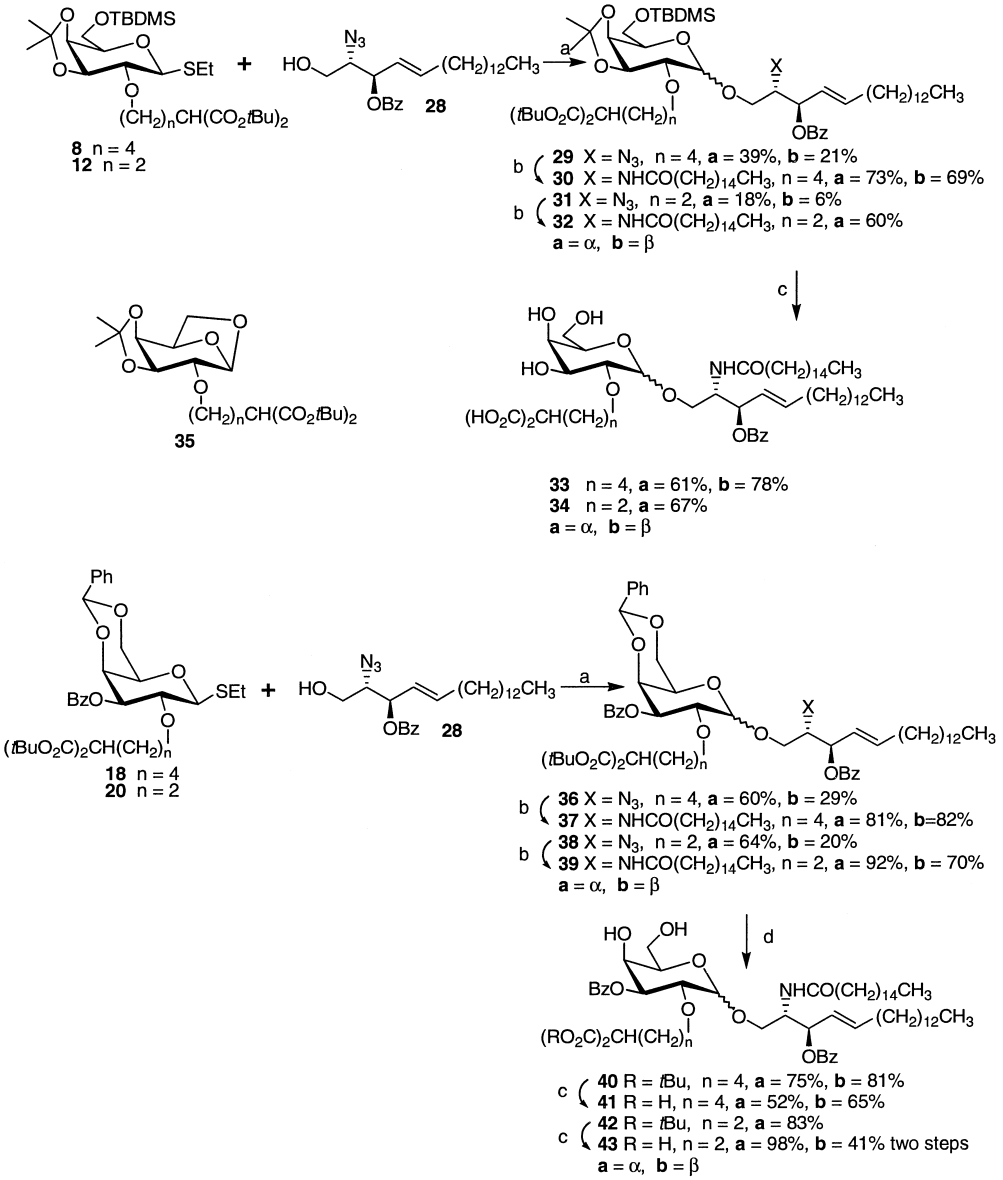
Scheme 2. (a) PMBCl, NaH, DMF; (b) AcOH, THF; (c) $PhCH(OCH_3)_2$, PTSA, MeCN; (d) Br-X-Br, NaH, DMF; (e) $NaCH(CO_2tBu)_2$, THF, DMF.

group and the t-butyl esters to provide the desired galactolipids **41a** and **b** and **43a** and **b**. The same synthetic scheme was followed for the preparation of analogues carrying Lemieux's lipopohilic entity (**60a** and **60b**).

3-Substituted galactoconjugates

Malonate substituted galactolipids in position 3 were prepared as reported in Schemes 2, 4, and 6. The non-participating paramethoxybenzyl ether protecting group in position 2 of the key ethyl 1-thio-galactopyranoside **26** and **27** (Scheme 2) was necesary since both α and β anomers were required for the study. This blocking group was also advantageously stable to alkylation conditions as well as acidic conditions. Hence, ethyl 1-thio-β-D-galactopyranoside **5** was alkylated with *p*-methoxybenzyl chloride to give compound **21**. Formation of the triol **22** was performed by mild acidic hydrolysis and the 4,6-benzylidene **23** was generated after reaction with benzaldehyde dimethylacetal. Sodium hydride treatment of **23** gave the corresponding 3-alkoxide which was alkylated by 1,4-dibromobutane or α-α′-dibromo-*p*-xylene. As for the 2-substituted analogues, the resulting bromides **25** or **27** were displaced by the anion of di-*t*-butyl malonate to give the desired intermediates **26** (X = $(CH_2)_4$) or **27** (X = $CH_2C_6H_4CH_2$).

3-Malonyl substituted galactocerebrosides **52** and **57** (Scheme 4) were both obtained after glycosidation of **26** and azido-sphingosine **28**. The coupling reaction gave a 3:2 mixture of the two anomers **44a** and **b** using dioxane as solvent. After separation of the anomers and usual reduction of the azido functionality followed by palmitic acid acylation, galactocerebrosides **45a** and **b** were obtained. Removal of the paramethoxybenzyl protecting group in position 2 was done with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and the resulting alcohols



Scheme 3. (a) DMTST, 2,6-di-*t*Bu-4-Me-pyridine, solvent, mol. sieves; (b) (1) H_2S, pyridine, H_2O; (2) $CH_3(CH_2)_{14}COCl$, NaOAc, THF; (c) TFA 90%; (d) TFA 90%, CH_2Cl_2.

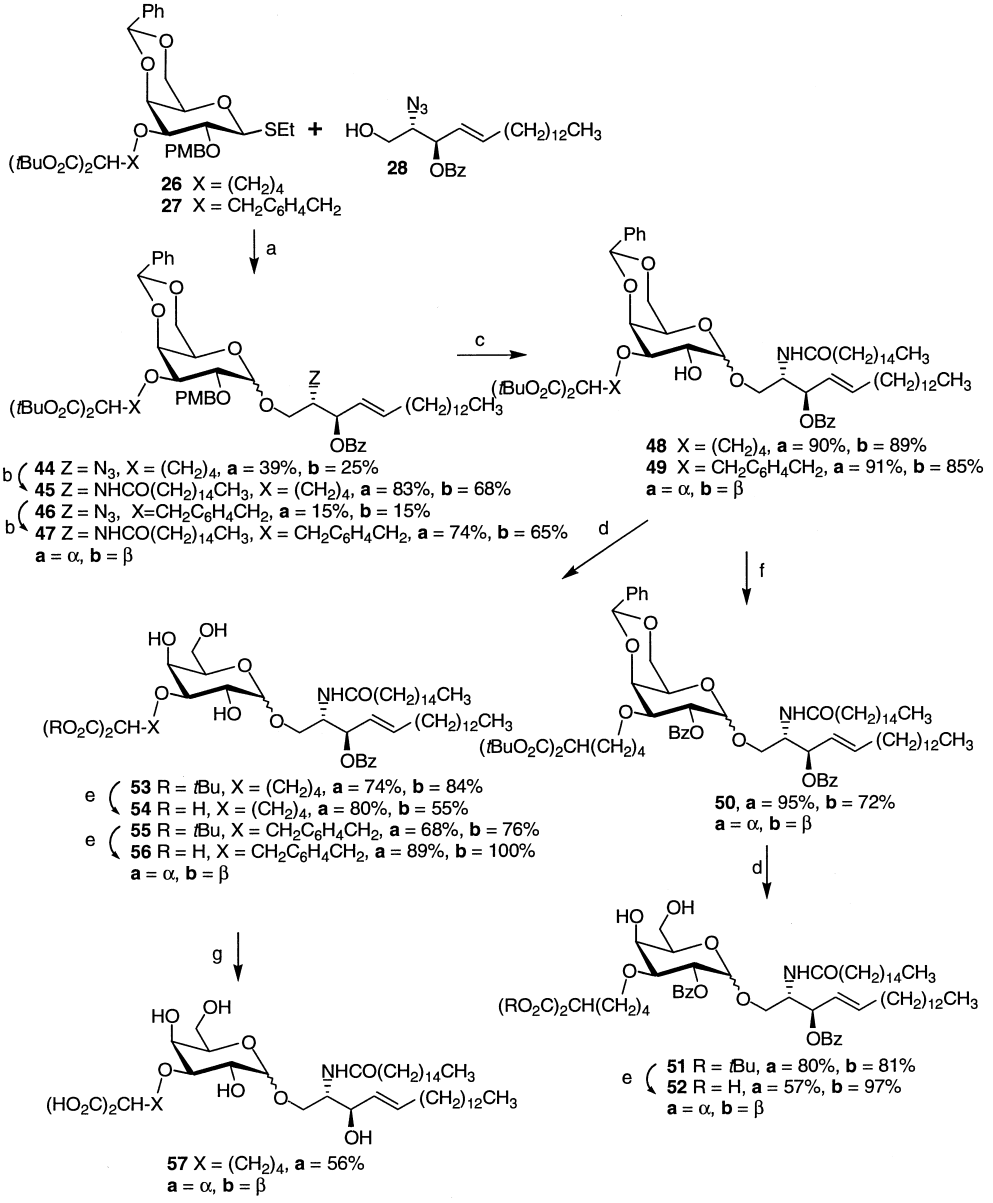
48a and **b** were then submitted to two successive acidic hydrolysis to liberate the 4- and 6-hydroxyls and recover the malonic acid functionality in **54a** and **b**. The same exact procedure was used to prepare the constrained galactocerebrosides **56a** or **b** which contain a methylbenzyl spacer. The key intermediate **27** was condensed with azido-sphingosine in acetonitrile and afforded a 1:1 mixture of α:β anomers **46a** and **b** which were easily separated by chromatography. Introduction of the acylamino side chain followed by removal of the benzylidene and the *tert*-butyl protecting groups gave the desired compounds **56a** or **b**.

On the other hand, the synthesis of benzoylated galactocerebrosides **52a** and **b** was achieved by benzoylation of alcohols **48a** and **b** followed by acidic hydrolysis of the resulting galactolipids **50a** and **b**. Galactoconjugates **66a** and **b** bearing the methoxycarbonyloctyl chain as lipid entity were obtained following a similar procedure as described in Scheme 6.

Biology

In vitro binding assays

Extravasation of neutrophils into sites of inflammation is dependent on the initial interaction with endothelial P-selectin. This is supported by in vitro evidence of leukocyte rolling on P-selectin in flow cells[30] as well as the in vivo anti-inflammatory activity of P-selectin blocking antibodies.[31] P-selectin is thus a novel target and an inhibitor may provide anti-inflammatory activity. Three assays have been put into place in order to determine the ability of compounds to inhibit the binding of P-selectin. Two employ a truncated soluble P-selectin

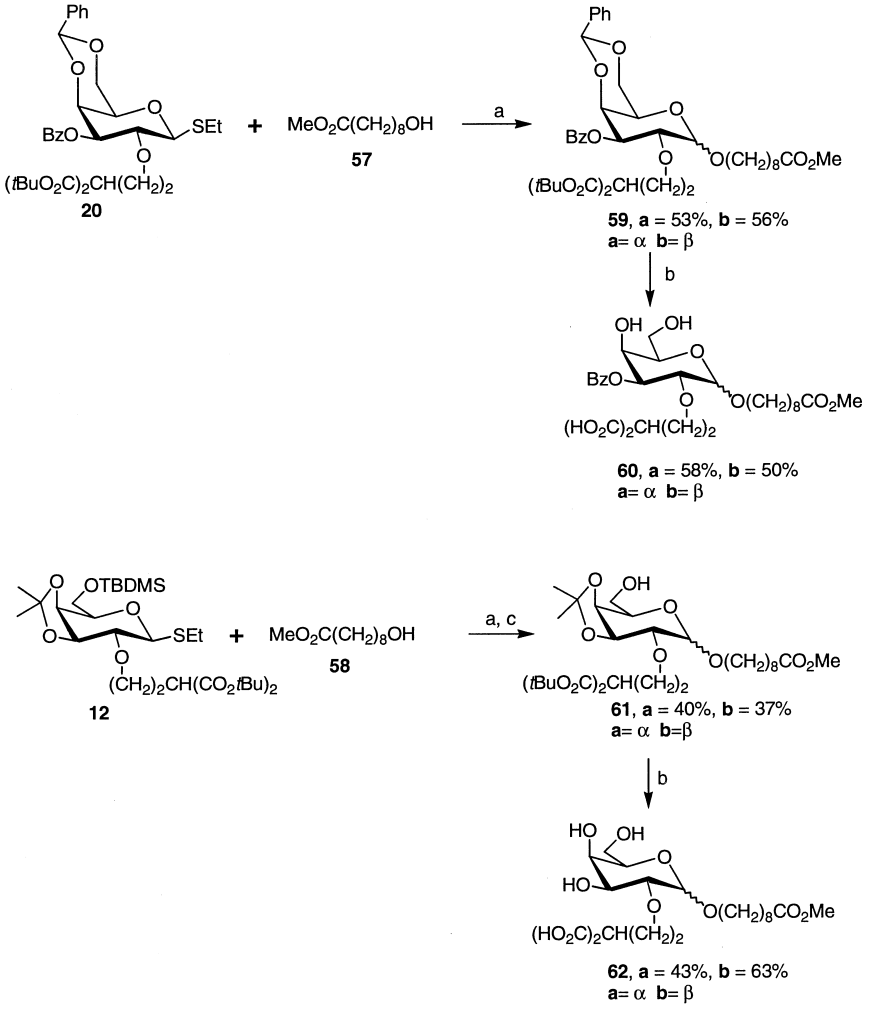


Scheme 4. (a) DMTST, 2,6-di-*t*Bu-4-Me-pyridine, solvent, mol. sieves; (b) (1). H_2S, pyridine, H_2O; (2) $CH_3(CH_2)_{14}COCl$, NaOAc, THF; (c) DDQ, CH_2Cl_2, H_2O; (d) TFA 90%, CH_2Cl_2, (e) TFA 90%; (f) BzCl, pyridine, DMAP; (g) MeONa.

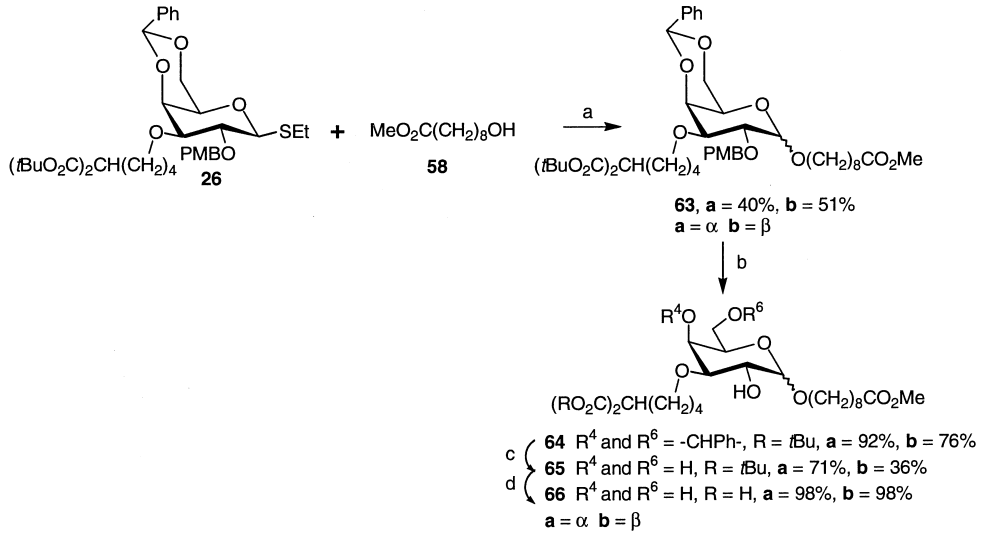
protein containing the lectin, EGF and two complement repeat domains fused to an immunoglobulin tail, termed receptor globulin (Rg), as described.[20,32] In a cell free assay, the P-selectin Rg was allowed to bind to a 96-well ELISA plate coated with sulfatides (Sigma). The P-selectin was bound to HRP-conjugated goat anti-human IgG and this immunocomplex was incubated on the antigen-coated plate in the presence or absence of the test compounds. The bound complexes were detected by addition of buffer containing substrate and 3,3′,5,5′-tetramethylbenzidine. Color development was monitored and following the termination of the assay, the absorbance at 450 nm was determined. The test compounds were compared to sulfatides (positive control) or solvent (negative control). The data was expressed as percent inhibition, from which an IC_{50} was calculated and reported in Table 1 as cell free data.

The second assay measures labeled HL-60 cells bound to immobilized P-selectin Rg. A 96-well plate was coated with anti-human IgG Fc antibody, non-specific binding sites were blocked with 1% non-fat dry milk, and P-selectin Rg was bound by the antibody. HL-60 cells (3×10^7 per mL of calcium and magnesium free phosphate buffered saline (PBS, Gibco) were labeled by taking up calcein acetoxymethyl ester (Molecular Probes) for 20 min followed by resuspension in complete PBS. In the assay, the P-selectin Rg coated wells were preincubated with an inhibitor for 15 min prior to addition of the labeled cells at 2×10^5 cells per 0.2 mL final volume. Following a 30 min binding period, the unbound cells were removed by aspiration and the bound cells were detected by a plate fluorimeter. The data were expressed as percent inhibition from which an IC_{50} value was determined and reported in Table 1 as HL-60:P-selRg data.

A third assay was also developed that employed HL-60 cells binding to thrombin-activated platelets that express P-selectin.[33] The platelets were labeled by incubation with calcein acetoxymethyl ester for 10 min at 37 °C. Without washing, the platelets were counted and the concentration adjusted to 1×10^7 per mL. The platelets were then activated with human thrombin, washed and resuspended in buffer and counted. Cell concentrations were adjusted to 2×10^7/mL for the platelets and 4×10^6 for HL-60 cells. The tested compounds were incubated with labeled platelets for 10 min before addition of HL-60 cells. The samples were analyzed on a flow cytometer by measuring the forward scatter and fluorescent intensity of the mixed cell population. The platelets appeared at lower forward scatter values and



Scheme 5. (a) DMTST, 2,6-di-*t*Bu-4-Me-pyridine, solvent, mol. sieves; (b) TFA 90%, anisole; (c) nBu$_4$NF, THF, AcOH.



Scheme 6.

were excluded. The percentage of HL-60 cells in fluorescent (containing bound platelets) and non-fluorescent populations was determined and plotted as a function of inhibitor concentration. The inhibition of binding was compared to standards which were treated with vehicle alone (0% inhibition) or incubated with EDTA (100% inhibition). IC_{50} values were calculated and reported as HL-60/platelet values in Tables 1–3.

In vivo testing

The in vivo test is a reverse passive Arthus reaction in rats[33] in which the interaction of antigen–antibody complexes and complement leads to a localized influx of neutrophils. These neutrophils release a variety of mediators that are associated with tissue damage and vascular permeability. E-selectin has been shown to be involved in the inflammation resulting from an Arthus reaction[33] but the role of P-selectin has not been determined. However it has been suggested that P-selectin is known to be involved in neutrophil dependent lung injury and P-selectin deficient mice exhibit delayed inflammatory reactions.[33]

The localized inflammation produced during a reverse passive Arthus reaction was evaluated by measuring the endpoints of vascular permeability (VP) and neutrophil infiltration (MPO). Briefly, the rats were administered intradermal injection of anti-BSA followed by intravenous injection of BSA containing ^{125}I labeled BSA to induce the inflammation reaction. Inhibitors of adhesion molecules were then administered intravenously and after 4 h, the rats were sacrificed. To assess changes in vascular permeability, the ^{125}I content of 15 mm punch biopsies was determined by gamma scintillation spectroscopy. The radioactivity in the tissue compared to the level of radioactive albumin in the blood at the time of sacrifice allows to calculate the plasma protein exudation into skin. The skin accumulation of neutrophils was determined from the tissue content of the marker enzyme myeloperoxidase (MPO). To measure the MPO content, the method of Bradley et al.[33,34] was used. The data were reported as the percent inhibition of the endpoint for a single dose of test compound (10 mg/kg, iv).

Results and Discussion

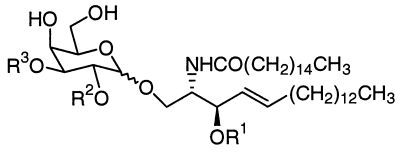
Table 1 compares a representative example of the malonate series (**43a**) with sLe^x, galactosyl ceramide and sulfatides. The sLe^x epitope had very poor inhibition of binding, as expected based on previous reports. Binding to sLe^x may depend on the presence of a clustered saccharide arrangement. The natural glycosylated polypeptide ligand from which sLe^x was released was presumed to create these multivalent saccharide patches that avidly recognize the selectins. It is noteworthy, however, that the commercial sulfatides did show

Table 1. In vitro and in vivo (RPA reaction) results of a selected malonate representative **43a** compared to commercial sulfatides (Aldrich), galactosylceramide and sLe^x

	In vitro Cell free IC_{50} (μM)	In vitro HL-60:PselRg IC_{50} (μM)	In vitro HL-60/platelet IC_{50} (μM)	In vivo RPA %inhibition VP	In vivo RPA %inhibition MPO
43a	8.2	49	12	41	96
sLe^x [a]	> 100	> 100	> 100		
Galactosyl ceramide	> 50	not active		0	0
Commercial Sulfatides (Sigma)	0.64	16		39.5	10

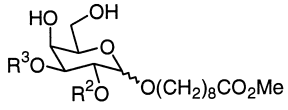
[a]As already mentioned, sLe^x affinity was shown to be ~0.5–1.0 mM, and therefore has not been tested at higher concentration than 100 μM in these assays.

Table 2. In vitro and in vivo (RPA reaction) results of various 2- and 3-malonate substituted galactocerebrosides as inhibitors of P-selectin



Compound	α/β	R^1	R^2	R^3	In vitro HL-60/Platelet IC_{50} (μM)	In vivo %inhibition VP	In vivo %inhibition MPO
33a	α	Bz	$(CH_2)_4CH(CO_2H)_2$	H	> 80		
33b	β	Bz	$(CH_2)_4CH(CO_2H)_2$	H	32	34	38
34a	α	Bz	$(CH_2)_2CH(CO_2H)_2$	H	> 100	0	14
41a	α	Bz	$(CH_2)_4CH(CO_2H)_2$	Bz	19	60	84
41b	β	Bz	$(CH_2)_4CH(CO_2H)_2$	Bz	8.8	4	62
43a	α	Bz	$(CH_2)_2CH(CO_2H)_2$	Bz	12	41	96
43b	β	Bz	$(CH_2)_2CH(CO_2H)_2$	Bz	8.5		
52a	α	Bz	Bz	$(CH_2)_4CH(CO_2H)_2$	9.6	0	9.6
52b	β	Bz	Bz	$(CH_2)_4CH(CO_2H)_2$	6		
54a	α	Bz	H	$(CH_2)_4CH(CO_2H)_2$	22.9	33	82
54b	β	Bz	H	$(CH_2)_4CH(CO_2H)_2$	45	16	31
56a	α	Bz	H	$CH_2C_6H_4CH_2$	1.3	43	77
56b	β	Bz	H	$CH_2C_6H_4CH_2$	2.9	17	77
57a	α	H	H	$(CH_2)_4CH(CO_2H)_2$	40.8		
Sulfatides (Sigma)	β	H	H	SO_3Na	2	39.5	10

Table 3. In vitro and in vivo (RPA reaction) results of various 2- and 3-malonate substituted galactoconjugates as inhibitors of P-selectin



Compound	R^2	R^3	In vitro HL-60:PselRg IC_{50} (μM)	In vitro HL-60/platelet IC_{50} (μM)	In vivo %inhibition VP	In vivo %inhibition MPO
60a	$(CH_2)_2CH(CO_2H)_2$	Bz	> 200	> 127		
60b	$(CH_2)_2CH(CO_2H)_2$	Bz	> 160	> 100	18	34
62a	$(CH_2)_2CH(CO_2H)_2$	H	172	> 150		
62b	$(CH_2)_2CH(CO_2H)_2$	H	> 100	> 150		
66a	Bz	$(CH_2)_4CH(CO_2H)_2$	159	> 145		
66b	Bz	$(CH_2)_4CH(CO_2H)_2$	73	> 145		
Sulfatides (Sigma)	H	SO_3Na	16	2	39.5	10

activity in both in vitro and in vivo assays. Even though sulfatides may coaggregate in patches on cell surfaces as is known for glycosphingolipids, these results show that the 'clustering' factor is not the only binding requirement for this type of compound. Galactosyl ceramide was inactive in these assays, despite the presence of the ceramide moiety. The potent inhibition by compound **43a** suggests that the combined structural features of this series are involved in the specific recognition of P-selectin.

Table 2 reports the results of all analogues bearing the sphingosine side-chain. As can be seen, several of the compounds are active in in vitro assays. Moreover, a number of these compounds showed activity when tested in vivo. By comparison with sulfatides as a reference, a number of the compounds showed superior in vivo activity. Derivatives **33a** and **34a** are the two compounds showing inactivity while analogues **54a**, **54b** and **57a** exhibits approximately 10- to 20-fold decrease in in vitro binding. However, in vivo activity, when compared to sulfatides, seems to be as good or even better for this type of compounds. Hence, although structurally different, the malonate substituted galactocerebrosides are favorably compared to the sulfatides.

In the 2-malonate substituted series, a rapid analysis of results concerning the two different spacers (**33a** vs **34a**, **41a** vs **43a** and **41b** vs **43b**) shows that similar activity was found and that chain length, in this range, does not seem to matter. The 4C spacer easily satisfies the 10 Å distance requirement that is approximately measured between Lys113 and the calcium ion in the binding cavity and one can imagine that its high flexibility can allow a slight folding in order to reach the two anchor

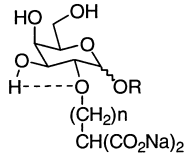


Figure 6. Internal H-bond in the non-benzoylated 2-malonate series.

points. On the other hand, it can be supposed that the 2C chain fulfills the required distance in a fully extended way. A marked effect of the benzoyl group in position 3 is apparent for this series of compounds (cf. compounds **41a** vs **33a**, **41b** vs **33b** and **34a** vs **43a**), improving their potency by 5-fold. This suggests the proximity of a lipophilic pocket in this region that provides a favorable interaction. One can also postulate the formation of an internal hydrogen bond between position 3 and 2 in the non-benzoylated analogues (cf. Fig. 6) that would affect the conformation of the sugar, its rigidity and consequently its orientation in the cavity. Other substituents at this position should be studied in order to get a clear idea of the reason of this behavior.

The effect of the anomeric center is not as clear. α-Configuration seems to slightly improve in vivo activity in the 3-benzoyl series (cf. compounds **41a** vs **41b** and **43a** vs **43b**), while β-configuration appears better in non-benzoylated compounds (**33b** vs **33a**). These results suggest that the position of the sugar in the pocket, which is controlled by the ceramide side-chain orientation, is not very critical in the case of benzoylated analogues since similar in vitro results are found. The flexibility of the ceramide moiety which may extend out from the protein's binding groove, could explain this behavior. Nevertheless, in the non-benzoylated series, a restricted sugar conformation due to an internal H-bond would support the large difference seen in in vitro activity between both anomers. The preference for a β-configuration obviously involves a critical binding orientation in the cavity for these compounds.

In the 3-malonate substituted series, a reverse effect was noticed concerning the presence of a benzoyl group on the sugar. Despite similar in vitro results, in vivo tests seem to indicate a deleterious effect of the presence of a 2-benzoyl as shown for compounds **52a** and **54a**. In this case, metabolism or transport issues are probably involved. Considering in vitro assays only, a preference for one of the anomers is not obvious in this series. However, in vivo testing indicates that in the non-benzoylated series (**54a** vs **54b**), the potency of the α-anomer is particularly enhanced. Again, bioavailability to the target tissue or metabolic instability of the β-anomer are implicated. The introduction of a rigid spacer between the acidic functionality and the carbohydrate ring in this series proved to be beneficial as shown by the in vitro results of **56a** and **56b** (by comparison with **54a** and **54b**). As in sLe^x, which is a relatively rigid molecule, selectin specificity gains are expected with constrained analogues such as **54a** and **b** which contain a methylbenzyl template. However, in vivo activity of these compounds, although very good, was not enhanced by the same magnitude. Similar results were found for both series which is not reflected in the in vitro activity.

Position comparison for the malonate substituted side-chain on the sugar must consider the presence of the benzoyl group. The absence of benzoyl clearly favors the 3-substituted analogues (**54a** vs **33a** and **34a**, **54b** vs **33b**) as indicated by both in vivo and in vitro biological tests. In contrast, benzoylated derivatives bearing a malonate side-chain in position 2 are equally active in vitro compared to the 3-substituted malonate compounds, but substantially more active in vivo (cf. compounds **41a** and **43a** vs **52a** and **52b** and **43b** vs **52b**). This comparison suggests that the benzoyl entity is tolerated in the cavity by both 2- and 3-malonate substituted derivatives. Benzoylation is also tolerated in vivo in the 2-malonate series. However, this substitution is a negative factor for in vivo activity in the 3-malonate series. Globally, the benzoylated 2-malonate analogues are the more potent as pointed in both in vitro and in vivo assays.

The biological results of derivatives bearing a methoxycarbonyloctyl aglycone chain[29] are presented in Table 3. Several key representatives shown in Table 2 were prepared with this moiety in order to assess the importance of the ceramide side-chain. The methoxycarbonyloctyl side chain, which was shown to enhance activity of sLe^x analogues[1] was proved to dramatically reduced the potency of this series of compounds. The only compound (**60b**) tested in vivo when compared to the corresponding cerebroside (**41b**) tends to show a similar behavior. The sphingosine aglycone thus plays an important role in the binding process. The size of the P-selectin pocket likely excludes any possibility of a sphingosine binding interaction with the protein. This large lipophilic entity is probably directed towards the solvent in a fully extended all-*trans* configuration as already known by X-ray crystallography or high-resolution NMR analysis of related compounds. The direction and the tilt of this part of the molecule is nevertheless unknown and might be important. Vesicles, micelles or bilayers can be formed with this lipidic moiety that would direct the polar sugar head in its pocket in a suitable way to interact with the binding features. Coaggregation in patches on cell surfaces could be a natural mechanism for generating specific selectin recognition in the case of the glycosphingolipids by mimicking the multivalent interactions that occur with the natural ligand.

Conclusion

The selectins are important mediators of inflammatory reactions. The discovery of a high-affinity selectin antagonist can lead to potent anti-inflammatory agents for the treatment of accute reactions. This study has shown the high-affinity binding of malonate substituted galactocerebrosides to P-selectin and their high potential as P-selectin antagonist. The 3-benzoylated 2-malonate galactocerebrosides, much more potent than sialyl Lewis X, have been identified as a lead in this new class of compounds.

The data presented in this study suggests that this new family of compounds acts by mimicking binding to the sLe^x binding pocket. This study has identified several key structural elements in this family of compounds. The malonate group at position 2 is clearly

favored as well as the presence of a substituent at position 3. The sphingosine side-chain is required for binding activity and the α-configuration is preferred, at least in vivo. Preliminary studies with a more rigid spacer as the methylbenzyl template indicate enhancement of activity in vitro. The introduction of rigidity in this class of molecules appears to be a promising approach to more optimally mimic the conformation of sLe^x and increase the binding affinity to P-selectin.

Experimental

Material and methods

Analytical grade solvents were used for reactions and chromatographies. Flash column chromatographies were performed on Merck silica gel 60 (230–400 mesh) and Merck silica gel 60 F_{254} 0.5 mm plates were used. All melting points were determined on a Gallenkamp metling point apparatus and were not corrected. ^{1}H NMR spectra were measured on a Bruker AC200 (200 MHz) or a Bruker AMX400 (400 MHz) instruments. Chemical shifts were reported in δ units using the solvent as internal standard. The abbreviations for the multiplicity are the following: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Infra-red spectras were recorded on a Perkin-Elmer 781 and optical rotations were measured on a Perkin-Elmer 241 apparatus. Elemental analysis were performed at the Analytical center of Bristol-Myers Squibb in Syracuse.

Key intermediates

Ethyl 3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside 5.[25] A mixture of ethyl 1-thio-β-D-galactopyranoside 4[24] (24.86 g, 0.111 mol) and 2,2-dimethoxypropane (500 mL) was treated with *p*-toluenesulfonic acid (0.625 g) and stirred at 22 °C for 24 h. Water (80 mL) was added and after 15 min the reaction mixture was cooled in an ice water bath and stirred for another 30 min. Then triethylamine (5 mL) was added and the mixture was stirred for 20 min. The solvent was evaporated under vacuum and the residue was purified by silica gel chromatography (9×12 cm, 50–70% ethyl acetate/toluene) to give the title material (25.50 g, 87%) as a white solid. Recrystallization from ethyl acetate and hexane gave white prisms (mp 90–93 °C). $[\alpha]_D^{22}$ +20.8° (*c* 2.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (3H, t, *J* = 7.3 Hz, $-SCH_2CH_3$), 1.36 and 1.52 (2×3H, 2s, $-C(CH_3)_2$), 2.2 and 2.5 (broad, OH), 2.75 (2H, m, $-SCH_2CH_3$), 3.57 (1H, dd, *J* = 10.2, 7.0 Hz, H-2), 3.81 (1H, dd, *J* = 11.5, 4.0 Hz, H-6), 3.89 (1H, m, H-5), 3.98 (1H, dd, *J* = 11.5, 7.2 Hz, H-6), 4.09 (1H, dd, *J* = 7.0, 5.6 Hz, H-3), 4.21 (1H, dd, *J* = 5.6, 2.2 Hz, H-4), 4.27 (1H, d, *J* = 10.2 Hz, H-1). IR (KBr) ν_{max} (cm^{-1}) 3200 (br, OH). Anal. calcd for $C_{11}H_{20}O_5S$: C, 49.98; H, 7.63; S, 12.13. Found: C, 49.89; H, 7.49; S, 12.35.

Ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside 6. A solution of ethyl 3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside **5** (8.65 g, 32.7 mmol) in dry pyridine (125 mL) was treated at 0–5 °C with *tert*-butyldimethylsilyl chloride (5.92 g, 39.2 mmol) and the resulting mixture was stirred for 5 h. Methanol (15 mL) was then added and the solution was stirred for another 15 min. The solvent was then evaporated under vacuum and the residue was diluted with ethyl acetate (500 mL) washed with cold 2 N hydrochloric acid, saturated sodium bicarbonate, brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent under vacuum gave an oil which was purified by chromatography on silica gel (9×11 cm, 10–20% ethyl acetate/toluene) and afforded the title compound (12.4 g, 100%) as an oil. $[\alpha]_D^{22}$ +2.8° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (6H, s, $Si(CH_3)_2$), 0.9 (9H, s,Si*t*Bu), 1.32 (3H, t, *J* = 7.5 Hz, $-SCH_2CH_3$) 1.35 and 1.53 (2×3H, 2s, $-C(CH_3)_2$), 2.7 (2H, m, $-SCH_2CH_3$), 3.56 (1H, dd, *J* = 10.2, 7.0 Hz, H-2), 3.8–3.9 (3H, m, H-5 and H-6), 4.05 (1H, dd, *J* = 7.0, 5.5 Hz, H-3), 4.24 (1H, d, *J* = 10.2 Hz, H-1) 4.26 (1H, dd, *J* = 5.5 and 2.0 Hz, H-4).

Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(4-bromobutyl)-1-thio-β-D-galactopyranoside 7. A stirred solution of ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside **6** (0.89 g, 2.35 mmol) in *N,N*-dimethylformamide (20 mL) was treated with sodium hydride (60% in mineral oil, 0.90 g, 22.5 mmol) at 0 °C. The mixture was stirred at room temperature for 10 min, then 1,4-dibromobutane (6 mL, 50.2 mmol) was added. The mixture was stirred for ~30 min at 22 °C, then diluted with ethyl ether and washed with saturated ammonium chloride, water and brine. The residue was purified by silica gel chromatography (5–8% ethyl acetate/hexane) to give the title compound (0.950 g, 79%) as an oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.07 (6H, s, $-Si(CH_3)_2$), 0.89 (9H, s, -Si*t*Bu), 1.29 (3H, t, *J* = 7.5 Hz, $-CH_2-CH_3$), 1.34 and 1.52 (6H, 2s, $-(CH_3)_2C-$), 1.67–1.80 and 1.92–2.06 (4H, 2m, $-(CH_2)_2-$), 2.62–2.82 (2H, m, $-SCH_2-$), 3.26 (1H, dd, *J* = 9.9, 6.7 Hz, H-2), 3.47 (2H, t, *J* = 6.7 Hz, $-CH_2Br$), 3.62–3.83 (4H, m, H-6 and $-OCH_2-$), 3.86 (1H, d, *J* = 1.9 Hz, H-5′), 4.07 (1H, dd, *J* = 5.5, 6.7 Hz, H-3), 4.22 (1H, dd, *J* = 5.5, 1.9 Hz, H-4), 4.32 (1H, d, *J* = 9.9 Hz, H-1). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 2940, 2920, 2840 (C–H).

Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside 8. A stirred solution of di-*tert*-butylmalonate (3.0 mL, 13.4 mmol) in tetrahydrofuran (20 mL) was treated with a solution of potassium *tert*-butoxide in *tert*-butanol (1.0 M, 15.0 mL, 15 mmol) at 0 °C. The mixture was stirred for ~30 min. A solution of ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-bromobutyl-1-thio-β-D-galactopyranoside **7** (4.00 g, 7.79 mmol) in *N,N*-dimethylformamide (20 mL) was then added to this mixture and the ice-cooled bath was removed. The mixture was heated to ~50–60 °C for ~2 h, then diluted with ethyl acetate. A saturated solution of ammonium chloride was added and the two phases were separated. The organic layer was then washed with water and brine, dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel

chromatography (5–10% ethyl acetate/hexane) and afforded the title compound (5.2 g, 100%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (6H, s, -Si(CH_3)$_2$), 0.90 (9H, s, -Si*t*Bu), 1.29 (3H, t, J = 7.4 Hz, -CH_2–CH_3), 1.34 (3H, s, -C(CH_3)$_2$-), 1.36–1.43 (2H, m, -CH_2-), 1.47 (18H, s, 2 ×-O*t*Bu), 1.52 (3H, s, -C(CH_3)$_2$-), 1.60–1.67 and 1.83 (4H, 2m, -(CH_2)$_2$-), 2.64–2.80 (2H, m, -SCH_2-), 3.13 (1H, t, -CH(CO_2tBu)$_2$), 3.28 (1H, dd, J = 9.8, 6.7 Hz, H-2), 3.65 (1H, dt, J = 9.3, 6.8 Hz, -OCH_2-), 3.72–3.79 and 3.82–3.89 (4H, 2m, -OCH_2-, H-5 and H-6), 4.09 (1H, br dd, H-3), 4.22 (1H, dd, J = 5.5, 2.0 Hz, H-4), 4.33 (1H, d, J = 9.8 Hz, H-1). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 2930, 2850 (C–H), 1740, 1725 (C=O).

Ethyl 6-*O*-*t*-butyldimethylsilyl-3,4-*O*-isopropylidene-2-*O*-*tert*-butyloxycarbonylmethyl-1-thio-β-D-galactopyranoside 9. A solution of ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside **6** (6.7 g, 17.7 mmol) in dimethylformamide (120 mL) was added to sodium hydride (4.25 g, 50% suspension in oil, previously washed with hexane, 88 mmol) under argon. The resulting suspension was stirred at 22 °C for 0.75 h. *tert*-Butyl bromoacetate (16.5 mL, 102 mmol) was added dropwise to this mixture, which was stirred for an additional h. The mixture was then diluted with cold 1 M aqueous sodium bicarbonate (150 mL) and ethyl acetate (250 mL). The organic phase was washed with water (4×150 mL), 1 M aqueous sodium bicarbonate (150 mL) and brine (150 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (300 g, 2–10% ethyl acetate/hexane) to give the title compound (8.03 g, 92%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s, -Si(CH_3)$_2$), 0.90 (9H, s, -Si*t*Bu), 1.30 (3H, t, J = 7.4 Hz, -CH_3), 1.33 and 1.50 (6H, 2s, -C(CH_3)$_2$), 1.48 (9H, s,-O*t*Bu), 2.67–2.82 (2H, m, -SCH_2-), 3.48 (1H, dd, J = 9.7, 6.0 Hz, H-2), 3.75 (1H, td, J = 6.6, 1.3 Hz, H-5), 3.82–3.89 (2H, m, H-6), 4.21 (1H, d, J = 16.2, -OCH_2CO-), 4.19–4.25 (2H, m, H-3 and H-4), 4.33 (1H, d, J = 16.2 Hz, -OCH_2CO-), 4.42 (1H, d, J = 9.7 Hz, H-1). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3055, 2990, 2835 (C–H), 1745 (C=O). Anal. calcd for $C_{23}H_{44}O_7SSi$: C, 56.06; H, 9.00; S, 6.51. Found: C, 56.20; H, 8.79; S, 6.67.

Ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-2-*O*-hydroxyethyl-1-thio-β-D-galactopyranoside 10. A solution of ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-2-*O*-*tert*-butyloxycarbonylmethyl-1-thio-β-D-galactopyranoside **9** (4.0 g, 8.1 mmol) in tetrahydrofuran (40 mL) was treated with lithium aluminium hydride (0.31 g, 8.1 mmol) which was added by portions at 5 °C. The reaction mixture was stirred for 1 h. The same quantity of lithium aluminium hydride is added again and the mixture was stirred for another h. The mixture was then diluted with ethyl ether, cooled down to −15 °C and treated with a 3 N aqueous solution of sodium hydroxide. This was stirred for 0.75 h, then the organic layer was separated and the residual gum was washed with ethyl ether (3×100 mL). The combined organic layers were then dried over anhydrous magnesium sulfate, filtered and concentrated. The residue (2.73 g, 80%) without any purification was used for the next reaction. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (6H, s, -Si(CH_3)$_2$), 0.90 (9H, s, -Si*t*Bu), 1.31 (3H, t, J = 7.4 Hz, -CH_3), 1.35 and 1.54 (6H, 2s, -C(CH_3)$_2$), 2.66–2.82 (2H, m, -SCH_2-), 2.92 (1H, t, J = 6.5 Hz, -OH), 3.55 (1H, dd, J = 10.0, 7.0 Hz, H-2), 3.63–3.74 (2H, m, -CH_2OH), 3.77 (1H, m, H-5), 3.82–3.90 (4H, m, -OCH_2- and H-6), 4.12 (1H, dd, J = 6.8, 5.5 Hz, H-3), 4.26 (1H, dd, J = 5.5, 2.1 Hz, H-4), 4.33 (1H, d, J = 10.0 Hz, H-1). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3490 (OH), 3050, 2990, 2935, 2860 (C-H). Anal. calcd for $C_{19}H_{38}O_6SSi$: C, 53.99; H, 9.06; S, 7.59. Found: C, 53.82; H, 8.91; S, 7.65.

Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-methanesulfonyloxyethyl-1-thio-β-D-galactopyranoside 11. Triethylamine (99 μL, 0.711 mmol) followed by methanesulfonyl chloride (44 μL, 0.569 mmol) were added to a stirred solution of ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-hydroxyethyl-1-thio-β-D-galactopyranoside **10** (0.200 g, 0.474 mmol) in methylene chloride (2 mL) at 0 °C. The mixture was stirred for 30 min then water (∼2 mL) was added. The aqueous layer was extracted with methylene chloride (3×3 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (30% ethyl acetate/hexane) and afforded the title compound (0.229 g, 97%) as an oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.07 (6H, s, -Si(CH_3)$_2$-), 0.89 (9H, s, Si*t*Bu), 1.28 (3H, t, J = 5.2 Hz, -CH_3), 1.33 and 1.52 (6H, 2s, -C(CH_3)$_2$), 2.72 (2H, m, -SCH_2-), 3.09 (3H, s, -SO_2CH_3), 3.31 (1H, dd, J = 9.9, 6.6 Hz, H-2), 3.74–4.17 (7H, m, H-6, H-5, -OCH_2- and -CH_2OMs), 4.24 (1H, dd, J = 5.4, 1.8 Hz, H-4), 4.35–4.41 (2H, m, H-1 and H-3).

Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside 12. *tert*-Butyl malonate (225 μL, 1.00 mmol) was added to a suspension of sodium hydride (36 mg, 80% suspension in oil, 1.20 mmol) in dimethylformamide (2 mL) at 0 °C. This mixture was stirred at 22 °C for 0.75 h, then a solution of ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-methanesulfonyloxy-ethyl-1-thio-β-D-galactopyranoside **11** (0.102 g, 0.204 mmol) in tetrahydrofuran (4 mL) was added in dropwise, followed by solid potassium iodide (∼7 mg, 0.04 mmol). The resulting mixture was stirred at 65 °C for 12 h, then diluted with ethyl acetate (∼10 mL) and quenched with saturated ammonium chloride. The organic layers were washed with water (10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (5–10% ethyl acetate/hexane) and afforded the title material (0.330 g, contaminated with *tert*-butyl malonate). An aliquot of pure material was purified and obtained as an oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.06 (6H, s, -Si(CH_3)$_2$), 0.88 (9H, s, -Si*t*Bu), 1.28 (3H, t, J = 3.2 Hz, -CH_3), 1.31 and 1.49 (6H, 2s, -C(CH_3)$_2$), 1.45 (18H, br s, 2×-O*t*Bu), 2.08 (2H, m, -CH_2–CH(CO_2tBu)$_2$), 2.70 (2H, m, -SCH_2-), 3.24 (1H, dd, J = 9.8, 6.6 Hz, H-2), 3.46 (1H, t, J = 7.4 Hz, -CH(CO_2tBu)$_2$), 3.63–3.85 (5H, m, H-5, H-6, -OCH_2-), 4.08 (1H, br t, H-3), 4.21 (1H, dd, J = 5.5, 1.8 Hz, H-4), 4.30 (1H, d, J = 9.8 Hz, H-1).

Ethyl 3,4-*O*-isopropylidene-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside 13. A solution of ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **8** (5.0 g, 7.7 mmol) in tetrahydrofuran (30 mL) was treated with tetra-butylammonium fluoride (3.09 mL, 1 M solution in tetrahydrofuran, 3.09 mmol) at 0 °C. The mixture was stirred at 22 °C for ~2 h, then diluted with ethyl acetate (~60 mL) and washed with water (~60 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography and gave the title compound (3.8 g, 86%) as an oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.19 (3H, t, J = 7.4 Hz, -CH_2-CH_3), 1.24–1.42 (23H, m, 2× -O*t*Bu, -CH_2-, -$C(CH_3)_2$-), 1.26 (3H, s, -$C(CH_3)_2$-), 1.47 (2H, ap q, -CH_2-), 1.67 (2H, ap q, -CH_2-), 2.63 (2H, m, -SCH_2-), 3.09 (1H, dd, J = 9.8, 6.8 Hz, H-2), 3.14 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.50–3.55 (3H, m, H-6 and -OCH_2-), 3.62 (1H, dt, J = 9.5, 6.2 Hz, -OCH_2-), 3.74 (1H, td, J = 6.3, 1.8 Hz, H-5), 4.05 (1H, br dd, H-3), 4.15 (1H, dd, J = 5.5, 1.9 Hz, H-4), 4.38 (1H, d, J = 9.8 Hz, H-1), 4.78 (1H, t, J = 5.6 Hz, -OH). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3700–3100 (OH), 2980, 2930, 2860 (C–H), 1745, 1725 (C=O).

Ethyl 2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside 15. A solution of ethyl 3,4-*O*-isopropylidene-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **13** (3.5 g, 6.1 mmol) in 80% acetic acid (20 mL) was stirred for ~72 h at 22 °C. The solvents were evaporated and the residue was purified by silica gel chromatography (0–5% methanol/ethyl acetate) to give the title compound (3.0 g, 99%) as an oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.19 (3H, t, J = 7.4 Hz, -CH_3), 1.36–1.24 (2H, m, -CH_2-), 1.40 (18H, s, 2× -O*t*Bu), 1.56–1.45 (2H, m, -CH_2-), 1.67 (2H, ap q, J = 7.7 Hz, -CH_2-), 2.62 (2H, m, -SCH_2-), 3.67–3.62, 3.57–3.52, 3.50–3.42, 3.40–3.29 and 3.15–3.11 (9H, 5 sets of m, H-2, H-3, H-4, H-5, H-6, -OCH_2- and -$CH(CO_2tBu)_2$), 4.24 (1H, d, J = 9.6 Hz, H-1), 4.48 (1H, d, J = 4.6 Hz, -OH), 4.54 (1H, t, J = 5.6 Hz, -OH-6), 4.78 (1H, d, J = 6.6 Hz, -OH). IR (nujol) ν_{max} (cm^{-1}): 3700–3000 (br, OH), 2910 (br, C–H), 1740, 1710 (C=O).

Ethyl 4,6-*O*-benzylidene-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside 17. A solution of ethyl 2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **15** (3.0 g, 6.05 mmol) in acetonitrile (50 mL) was treated with benzaldehyde dimethylacetal (4.5 mL, 30.3 mmol) and *p*-toluenesulfonic acid (150 mg). The mixture was stirred at 22 °C for 1 h, then was diluted with ethyl acetate (50 mL) and washed with aqueous 1 M sodium bicarbonate (~50 mL) and brine (~50 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (30–50% ethyl acetate/hexane) and afforded the title material (2.1 g, 59%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, t, J = 7.5 Hz, -CH_2-CH_3), 1.37–1.49 (2H, m, -CH_2-), 1.46 (18H, 2s, 2×-O*t*Bu), 1.62–1.68 and 1.78–1.87 (4H, 2m, -$(CH_2)_2$-), 2.71–2.86 (3H, m, -SCH_2- and -OH), 3.13 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.43–3.48 (2H, m, H-2 and H-5), 3.68 (1H, dd, J = 8.4, 3.6 Hz, H-3), 3.70–3.77 (1H, m, -OCH_2-), 3.84 (1H, dt, J = 8.8, 6.4 Hz, -OCH_2-), 4.03 (1H, dd, J = 12.4, 1.7 Hz, H-6), 4.26 (1H, d, J = 3.5 Hz, H-4), 4.34 (1H, dd, J = 12.4, 1.3 Hz, H-6), 4.36 (1H, d, J = 9.5 Hz, H-1), 5.55 (1H, s, -OCHO-), 7.37–7.41 and 7.51–7.53 (5H, 2 sets of m, aromatic H).

Ethyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside 18. A stirred solution of ethyl 4,6-*O*-benzylidene-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **17** (2.1 g, 3.56 mmol) in methylene chloride (20 mL) and pyridine (20 mL) was treated with benzoyl chloride (530 μL, 4.58 mmol) and 4-dimethylaminopyridine (~10 mg) at 22 °C. The mixture was stirred for 4 h then diluted with methylene chloride (40 mL) and washed with aqueous 1 M sodium bicarbonate (~40 mL) and brine (~40 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (10–30% ethyl acetate/hexane) and gave the title material (2.1 g, 85%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18–1.30 (2H, m, -CH_2-), 1.34 (3H, t, J = 7.5 Hz, -CH_2–CH_3), 1.42 and 1.43 (18H, 2s, 2× -O*t*Bu), 1.48–1.54 (2H, m, -CH_2-), 1.60–1.73 (2H, m, -CH_2-), 2.73–2.90 (2H, m, -SCH_2-), 2.95 (1H, t, J = 7.6 Hz, -$CH(CO_2tBu)_2$), 5.58 (1H, br s, H-5), 3.64 (1H, dt, J = 8.9, 6.6 Hz, -OCH_2-), 3.81 (1H, dt, J = 8.9, 6.7 Hz, -OCH_2-), 3.85 (1H, t, J = 9.6 Hz, H-2), 4.03 (1H, dd, J = 12.4, 1.6 Hz, H-6), 4.36 (1H, dd, J = 12.4, 1.3 Hz, H-6), 4.50 (1H, d, J = 3.5 Hz, H-4), 4.51 (1H, d, J = 9.5 Hz, H-1), 5.14 (1H, dd, J = 9.6, 3.5 Hz, H-3), 5.50 (1H, s, -OCHO-), 7.35–7.39, 7.44–7.50, 7.55–7.60 and 8.07–8.09 (10H, 4 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 2970, 2920, 2860 (C–H), 1740, 1720 (C=O).

Ethyl 3,4-*O*-isopropylidene-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside 14. Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside **12** (0.330 g, contaminated with *tert*-butyl malonate) was reacted by the procedure used to synthesized compound **13** and gave the title compound (0.069 g, 67% for 2 steps) as an oil. $[\alpha]_D^{22}$ –1.2° (*c* 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (3H, t, J = 7.7 Hz, -CH_3), 1.34 and 1.51 (6H, 2s, -$C(CH_3)_2$), 1.47 (18H, s, 2× -O*t*Bu), 2.05–2.12 (3H, m, -$CH_2CH(CO_2tBu)_2$ and -OH), 2.74 (2H, m, -SCH_2-), 3.28 (1H, dd, J = 9.5 and 6.2 Hz, H-2), 3.47 (1H, t, J = 7.4 Hz, -$CH(CO_2tBu)_2$), 3.68 (1H, dt, J = 9.6, 6.3 Hz, -OCH_2-), 3.76–3.84 and 3.92–3.99 (4H, 2 sets of m, -OCH_2-, H-6 and H-5), 4.14 (1H, br dd, H-3), 4.18 (1H, dd, J = 5.8, 1.7 Hz, H-4), 4.35 (1H, d, J = 9.5 Hz, H-1). IR (film) ν_{max} (cm^{-1}) 3700–3020 (OH), 2970, 2920 (C-H), 1720 (C=O). Anal. calcd for $C_{24}H_{42}O_9S$: C, 56.90; H, 8.36; S, 6.33. Found: C, 56.83; H, 8.14; S, 6.59.

Ethyl 2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside 16. A solution of ethyl 3,4-*O*-isopropylidene-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside **14** (0.885 g, 1.75 mmol) in tetrahydrofuran (20 mL) was treated with aqueous

hydrochloric acid (2 N, 5 mL). The mixture was stirred at 22 °C for 12 h and then diluted with ethyl acetate (25 mL). Solid sodium bicarbonate was added at 0 °C, followed by anhydrous magnesium sulfate. The mixture was filtered and the solvents were evaporated. The residue was purified by silica gel column chromatography (30% ethyl acetate/hexane to pure ethyl acetate) to give the title compound (0.758 g, 93%) as an oil. $[\alpha]_D^{22}$ −25.9° (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.32 (3H, t, *J* = 7.5 Hz, -CH_3), 1.47 and 1.48 (18H, 2s, 2× -O*t*Bu), 1.98–2.06 (1H, m, -OH), 2.15–2.28 (2H, m, -C*H*$_2$CH(CO_2tBu)$_2$), 2.76 (2H, m, -SCH_2-), 2.80 (1H, br s, -OH), 3.34 (1H, br dd, H-2), 3.45–3.54 (3H, m, H-5, -CH(CO_2tBu)$_2$ and -OCH_2-), 3.59 (1H, td, *J* = 8.8 and 3.3 Hz, -OCH_2-), 3.82 (1H, ddd, *J* = 11.8, 8.4 and 4.3 Hz, H-6), 3.97 (1H, ddd, *J* = 11.8, 6.6 and 4.4 Hz, H-6), 4.04 (1H, d, *J* = 1.2 Hz, -OH-4), 4.17 (1H, dd, *J* = 8.9 and 4.4 Hz, H-3), 4.31 (1H, d, *J* = 9.7 Hz, H-1), 4.38 (1H, br d, *J* = 3.2 Hz, H-4). IR (film) ν_{max} (cm^{-1}) 3700–3020 (OH), 2970, 2920 (C–H), 1720 (C=O). Anal. calcd for $C_{21}H_{38}O_9S.0.3H_2O$: C, 53.44; H, 8.24; S, 6.79. Found: C, 53.39; H, 7.95; S, 6.76.

Ethyl 2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside 19. Ethyl 2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside **16** (0.724 g, 1.55 mmol) in acetonitrile (20 mL) was reacted by the procedure used to synthesize compound **17** and afforded the title material (0.77 g, 89%) as an oil. $[\alpha]_D^{22}$: −32.8° (*c* 1.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, t, *J* = 7.5 Hz, -CH_3), 1.45 and 1.46 (18H, 2s, 2×-O*t*Bu), 2.02–2.21 (2H, m, -C*H*$_2$–CH(CO_2tBu)$_2$), 2.79 (2H, m, -SCH_2-), 3.44 (1H, br s, H-5), 3.46–3.51 (2H, m, -CH(CO_2tBu)$_2$ and H-2), 3.55 (1H, *J* = 6.4 Hz, -OH), 3.64–3.69 and 4.05–4.08 (3H, 2 sets of m, H-3 and -OCH_2-), 4.03 (1H, dd, *J* = 12.7, 1.7 Hz, H-6), 4.26 (1H, d, *J* = 3.5 Hz, H-4), 4.32 (1H, d, *J* = 9.5 Hz, H-1), 4.32 (1H, d, *J* = 12.7 Hz, H-6), 5.55 (1H, s, -OCHO-), 7.35–7.39 and 7.50–7.53 (5H, 2 sets of m, -C_6H_5). IR (film) ν_{max} (cm^{-1}) 3600–3200 (OH), 2970, 2920, 2880 (C–H), 1735, 1720 (C=O). Anal. calcd for $C_{28}H_{42}O_9S$: C, 60.63; H, 7.63; S, 5.78. Found: C, 60.74; H, 7.46; S, 6.23.

Ethyl 2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside 20. Ethyl 2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside **19** (0.751 g, 1.35 mmol) in methylene chloride (8 mL) and pyridine (7 mL) was reacted by the procedure used to synthesize compound **18** and gave the title material (0.888 g, 99%) as an oil. $[\alpha]_D^{22}$ +51° (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (3H, t, *J* = 7.6 Hz, -CH_3), 1.37 and 1.42 (18H, 2s, 2×-O*t*Bu), 2.00 (2H, m, -C*H*$_2$–CH(CO_2tBu)$_2$), 2.82 (2H, m, -SCH_2-), 3.37 (1H, dd, *J* = 7.9, 6.6 Hz, -CH(CO_2tBu)$_2$), 3.58 (1H, br s, H-5), 3.75 (1H, dt, *J* = 9.2, 5.9 Hz, -OCH_2-), 3.81–3.87 (1H, m, -OCH_2-), 3.87 (1H, dd, *J* = 9.6, 9.6 Hz, H-2), 4.03 (1H, dd, *J* = 12.4, 1.6 Hz, H-6), 4.36 (1H, dd, *J* = 12.4, 1.3 Hz, H-6), 4.50 (1H, d, *J* = 9.6 Hz, H-1), 4.53 (1H, d, *J* = 3.5 Hz, H-4), 5.12 (1H, dd, *J* = 9.6, 3.5 Hz, H-3), 5.49 (1H, s, -OCHO-), 7.34–7.38, 7.43–7.48, 7.56–7.60 and 8.08–8.10 (10H, 4 sets of m, 2×-C_6H_5). IR (film) ν_{max} (cm^{-1}) 3035, 3010, 2970, 2920, 2860 (C–H), 1720 (C=O). Anal. calcd for $C_{35}H_{46}O_{10}S$: C, 63.81; H, 7.04; S, 4.87. Found: C, 63.94; H, 6.89; S, 5.41.

Ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-2-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside 21. A solution of ethyl 6-*O*-*tert*-butyl-dimethylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside **6** (12.4 g, 32.7 mmol) in *N,N*-dimethylformamide (45 mL) was added to a suspension of sodium hydride (1.35 g of 80% in mineral oil, 45.0 mmol) in *N,N*-dimethylformamide (90 mL) and the resulting mixture was stirred at 22 °C for 2 h. The reaction mixture was then cooled to 0–5 °C, treated dropwise with *p*-methoxybenzyl chloride (8.1 mL, 59.8 mmol) and stirred at 22 °C for 2 h. The reaction mixture was cooled again in an ice bath and treated dropwise with water (20 mL). The reaction mixture was then diluted with water (300 mL) and extracted with ether (3×300 mL). The combined extracts were washed with brine, dried over anhydrous magnesium sulfate and evaporated. The residual oil was purified on silica gel chromatography (9×12 cm, 0–10% ethyl acetate/toluene) and gave the title compound (10.5 g, 64%) as an oil. ^1H NMR (200 MHz, $CDCl_3$) δ 0.06 (6H, s, $SiCH_3$), 0.88 (9H, s, -Si*t*Bu), 1.29 (3H, t, *J* = 7.4 Hz, -SCH_2CH_3), 1.34 and 1.44 (2×3H, 2s, -C(CH_3)$_2$), 2.7 (2H, m, -SCH_2CH_3), 3.41 (1H, dd, *J* = 6.1, 9.9 Hz, H-2), 3.79 (3H, s, -OCH_3), 3.7–3.9 (3H, m, H-5 and H-6), 4.15–4.25 (2H, m, H-3 and H-4 overlapping), 4.39 (1H, d, *J* = 9.9 Hz, H-1), 4.70 (1H, d, *J* = 11.0 Hz, -OCH_2Ar), 4.74 (1H, d, *J* = 11.0 Hz, -OCH_2Ar), 6.86 (2H, d, *J* = 8.7 Hz, H-3 of 4-methoxybenzyl) and 7.35 (2H, d, *J* = 8.7 Hz, H-2 of 4-methoxybenzyl). IR (NaCl, film) ν_{max} (cm^{-1}) 1612 (aromatic) and 1516.

Ethyl 2-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside 22. A solution of ethyl 6-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-2-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside **21** (10.50 g, 21.05 mmol) in 80% aqueous acetic acid (100 mL) was heated at 60 °C for 1.5 h. The cooled mixture was evaporated under vacuum and the last traces of acetic acid removed by co-evaporation with toluene. Chromatography of the residue on silica gel (7×13 cm, 0–10% methanol/chloroform) gave the title compound (5.67 g, 78%) as a solid. Recrystallization from dichloromethane gave a white solid; mp 131–132 °C. $[\alpha]_D^{22}$ +22.7° (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (3H, t, *J* = 7.5 Hz, -SCH_2CH_3), 2.22 (1H, m, -OH), 2.50 (1H, d, *J* = 4.4 Hz, -OH), 2.73–2.87 (3H, m, OH and -SCH_2CH_3), 3.5–3.6 (2H, m, H-2 and H-5 overlapping), 3.61 (1H, m, H-3), 3.82 (3H, s, -OCH_3), 3.84 (1H, m, H-6), 3.95 (1H, m, H-6), 4.03 (1H, br s, H-4), 4.44 (1H, d, *J* = 9.4 Hz, H-1), 4.63 and 4.92 (2H, 2d, *J* = 10.8 Hz, -OCH_2Ar), 6.91 (2H, d, *J* = 8.6 Hz, H-3 of 4-methoxybenzyl) and 7.34 (2H, d, *J* = 8.6 Hz, H-2 of 4-methoxybenzyl). IR (KBr) ν_{max} (cm^{-1}): 3500 and 3300 (broad, OH) and 1605 (aromatic). Anal. calcd for $C_{16}H_{24}O_6S$: C, 55.80; H, 7.02; S, 9.31. Found: C, 55.64; H, 6.78; S, 9.23.

Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-1-thio-β-D-galactopyranoside 23. Ethyl 2-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside **22** (6.11 g, 17.7 mmol) in

acetonitrile was reacted by the procedure used to synthesize compound **17** and afforded the title compound (4.72 g, 62%) as a colorless oil. $[\alpha]_D^{22}$ +14.1° (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (3H, t, *J* = 7.4 Hz, -CH_3), 2.52 (1H, d, *J* = 8.3 Hz, -OH), 2.81 (2H, m, -SCH_2-), 3.47 (1H, br d, H-5), 3.64 (1H, dd, *J* = 9.2, 9.2 Hz, H-2), 3.77 (1H, m overlapped by -OCH_3, H-3), 3.80 (3H, s, -OCH_3), 4.03 (1H, dd, *J* = 12.5, 1.7 Hz, H-6), 4.25 (1H, d, *J* = 3.5 Hz, H-4), 4.35 (1H, dd, *J* = 12.5, 1.2 Hz, H-6), 4.44 (1H, d, *J* = 9.5 Hz, H-1), 4.72 (1H, d, *J* = 10.3 Hz, -OCH_2Ar), 4.88 (1H, d, *J* = 10.3 Hz, -OCH_2Ar), 5.57 (1H, s, -OCHO-), 6.87–6.92, 7.15–7.19, 7.25–7.32, 7.36–7.43 and 7.50–7.54 (9H, 5 sets of m, aromatic H). IR (KBr) ν_{max} (cm^{-1}) 3600–3250 (broad, OH) and 1610, 1510 (aromatic C=C). Anal. calcd for $C_{23}H_{28}O_6S.0.2\ H_2O$: C, 63.34; H, 6.56. Found: C, 63.42; H, 6.40.

Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-(4-bromobutyl)-1-thio-β-D-galactopyranoside 24. Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-1-thio-β-D-galactopyranoside **23** (3.5 g, 8.1 mmol) was reacted by the procedure used to synthesize compound **7** and afforded the title compound (2.7 g, 59%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (3H, t, *J* = 7.5 Hz, -CH_3), 1.76–1.82 and 1.96–2.03 (2×2H, 2 sets of m, -$(CH_2)_2$-), 2.81 (2H, m, -SCH_2-), 3.38–3.44 (3H, m, H-5 and -CH_2Br), 3.46 (1H, dd, *J* = 9.1, 3.2 Hz, H-3), 3.61 (1H, dt, *J* = 9.2, 6.0 Hz, -OCH_2-), 3.75 (1H, dt, *J* = 9.2, 6.1 Hz, -OCH_2-), 3.78 (1H, br dd, H-2), 3.81 (3H, s, -OCH_3), 4.03 (1H, dd, *J* = 12.3, 1.6 Hz, H-6), 4.32 (1H, d, *J* = 3.2 Hz, H-4), 4.36 (1H, dd, *J* = 12.3, 1.3 Hz, H-6), 4.44 (1H, d, *J* = 9.6 Hz, H-1), 4.72 (1H, d, *J* = 9.8 Hz, -OCH_2Ar), 4.81 (1H, d, *J* = 9.8 Hz, -OCH_2Ar), 5.55 (1H, s, -OCHO-), 6.87–6.90, 7.33–7.41 and 7.52–7.55 (9H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3050, 2980 (C–H), 1610, 1515 (aromatic C=C). Anal. calcd for $C_{27}H_{35}O_6SBr$: C, 57.14; H, 6.22. Found: C, 57.38; H, 6.14.

Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-(4-bromomethylphenyl)-1-thio-β-D-galactopyranoside 25. Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-1-thio-β-D-galactopyranoside **23** (1.03 g, 2.38 mmol)) was reacted by the procedure used to synthesize compound **7** except that dibromoxylene was used instead of dibromobutane. This afforded the title compound (0.92 g, 61%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (3H, t, *J* = 7.5 Hz, -SCH_2CH_3), 2.81 (2H, m, -SCH_2-), 3.37 (1H, s, H-5), 3.57 (1H, dd, *J* = 9.2, 3.5 Hz, H-3), 3.82 (3H, s, -OCH_3), 3.88 (1H, dd, *J* = 9.4, 9.4 Hz, H-2), 3.98 (1H, dd, *J* = 12.3, 1.6 Hz, H-6), 4.18 (1H, d, *J* = 3.4 Hz, H-4), 4.32 (1H, dd, *J* = 12.3, 1.3 Hz, H-6), 4.43 (1H, d, *J* = 9.6 Hz, H-1), 4.50 (2H, s, -CH_2Br), 4.75 and 4.84 (2× 1H, 2 d, *J* = 9.8 Hz, -OCH_2Ar), 4.76 (2H, s, -OCH_2- of *p*-bromomethylbenzyl), 5.49 (1H, s, -OCHO-), 6.86–6.89, 7.34–7.42 and 7.54–7.56 (13H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980 (C-H).

Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside 26. Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-(4-bromobutyl)-1-thio-β-D-galactopyranoside **24** (1.5 g, 2.64 mmol) was reacted by the procedure used to synthesize compound **8** and afforded the title compound (1.52 g, 82%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, t, *J* = 7.5 Hz, -CH_3), 1.45 (18H, s, 2×-O*t*Bu), 1.58, 1.68 and 1.83 (3×2H, -$(CH_2)_3$-), 2.80 (2H, m, -SCH_2-), 3.10 (1H, t, *J* = 7.5 Hz, -$CH(CO_2t Bu)_2$), 3.42 (1H, br s, H-5), 3.45 (1H, dd, *J* = 9.2, 3.5 Hz, H-3), 3.59 (1H, dt, *J* = 9.2, 6.6 Hz, -OCH_2-), 3.71 (1H, dt, *J* = 9.2, 6.7 Hz, -OCH_2-), 3.76–3.84 (1H, m overlapped by -OCH_3, H-2), 3.81 (3H, s, -OCH_3), 4.03 (1H, dd, *J* = 12.3, 1.5 Hz, H-6), 4.30 (1H, d, *J* = 3.4 Hz, H-4), 4.34 (1H, dd, *J* = 12.3, 1.2 Hz, H-6), 4.43 (1H, d, *J* = 9.6 Hz, H-1), 4.74 (1H, d, *J* = 9.9 Hz, -CH_2OAr), 4.78 (1H, d, *J* = 9.9 Hz, -OCH_2Ar), 5.54 (1H, s, -OCHO-), 6.85–6.92, 7.30–7.40 and 7.49–7.54 (9H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980 (C–H), 1740, 1720 (C=O). Anal. calcd for $C_{38}H_{54}O_{10}S$: C, 64.93; H, 7.74. Found: C, 64.94; H, 7.64.

Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-1-thio-β-D-galactopyranoside 27. Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-(4-bromobutyl)-1-thio-β-D-galactopyranoside **24** (0.714 g, 3.3 mmol) was reacted by the procedure used to synthesize compound **8** and afforded the title compound (0.922 g, 82%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, t, *J* = 7.5 Hz, -SCH_2CH_3), 1.42 (2×9H, 2 s, 2×-O*t*Bu), 2.80 (2H, m, -SCH_2-), 3.13 (2H, d, *J* = 7.8 Hz, -CH_2-$CH(CO_2t Bu)_2$), 3.34 (1H, s, H-5), 3.45 (1H, t, *J* = 7.8 Hz, -$CH(CO_2t Bu)_2$), 3.55 (1H, dd, *J* = 9.2, 3.4 Hz, H-3), 3.82 (3H, s, -OCH_3), 3.87 (1H, dd, *J* = 9.3, 9.3 Hz, H-2), 3.97 (1H, d, *J* = 12.3 Hz, H-6), 4.12 (1H, d, *J* = 3.3 Hz, H-4), 4.31 (1H, d, *J* = 12.3 Hz, H-6), 4.42 (1H, d, *J* = 9.6 Hz, H-1), 4.67–4.84 (4H, m, 2×-OCH_2Ar), 6.87–6.89, 7.16–7.18, 7.27–7.41 and 7.54–7.56 (13H, 4 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980 (C–H), 1740, 1720 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-4-octadecene 33a

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene 29a and **(2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyloxy]-4-octadecene 29b**. A solution of ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **8** (1.0 g, 1.54 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (0.627 g, 3.08 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-benzoyloxy-4-octadecen-1-ol **28**[27] (0.640 g, 1.48 mmol) in toluene (12 mL) was stirred with molecular sieves (4 Å, previously heated with a Bunsen flame) for 1 h at 22 °C. Then dimethyl(methylthio)sulfonium triflate (0.765 g, 3.08 mmol) was added in and stirring was continued for 1 h. The mixture was diluted with ethyl acetate (12 mL) and filtered through Celite. The filtrate was washed with 1 M aqueous sodium bicarbonate (12 mL) and brine (12 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was

purified by silica gel column chromatography (5–30% ethyl acetate/hexane) and gave the α-anomer (0.595 g, 39%) and the β-anomer (0.321 g, 21%) of the title compound as oils. **α-Anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (6H, s, -Si(CH_3)$_2$), 0.89 (3H, t, J = 7.0 Hz, -CH_3), 0.91 (9H, s, -Si*t*Bu), 1.25–1.51 and 1.58–1.66 (26H, 2 sets of m, -(CH_2)$_{11}$- and -(CH_2)$_2$-), 1.45 (18H, s, 2×-O*t*Bu), 1.33 and 1.51 (2×3H, 2 s, -C(CH_3)$_2$-), 1.81 and 2.07 (2×2H, 2 ap q, =CH-CH_2- and -CH_2–CH(CO_2tBu)$_2$), 3.11 (1H, t, J = 7.5 Hz, -CH(CO_2tBu)$_2$), 3.44 (1H, dd, J = 6.9, 3.4 Hz, H-2′), 3.52 (1H, dd, J = 10.8, 8.0 Hz, H-1), 3.61 (2H, t, J = 6.7 Hz, -OCH_2-), 3.78 (1H, dd, J = 10.0, 6.6 Hz, H-6′), 3.83–3.88 (2H, m, H-1 and H-6′), 3.99 (1H, m, H-2), 4.04 (1H, td, J = 6.5, 2.0 Hz, H-5′), 4.21 (1H, dd, J = 5.6, 2.2 Hz, H-4′), 4.20–4.26 (1H, m overlapped by H-4′, H-3′), 4.91 (1H, d, J = 3.4 Hz, H-1′), 5.54–5.61 (2H, m, H-3 and H-4), 5.93 (1H, dt, J = 14.1 and 6.8 Hz, H-5), 7.44–7.48, 7.56–7.60 and 8.06–8.08 (5H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3050, 2980, 2930, 2855 (C-H), 2105 (-N_3), 1720 (C=O). Anal. calcd for $C_{55}H_{93}N_3O_{13}Si$: C, 64.99; H, 9.22; N, 4.13. Found: C, 65.05; H, 8.97; N, 4.23. **β-Anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s, -Si(CH_3)$_2$), 0.89 (12H, m, -Si*t*Bu and -CH_3), 1.25–1.52 and 1.61–1.68 (26H, 2 sets of m, -(CH_2)$_{11}$- and -(CH_2)$_2$-), 1.33 and 1.53 (2×3H, 2 s, -C(CH_3)$_2$-), 1.45 (18H, s, 2×-O*t*Bu), 1.83 (2H, ap q, J = 7.8 Hz, -CH_2-CH(CO_2tBu)$_2$), 2.07 (2H, ap q, J = 6.9 Hz, =CH-CH_2-), 3.13 (1H, br t, H-2′), 3.25 (1H, t, J = 7.4 Hz, -CH(CO_2tBu)$_2$), 3.57 (1H, dd, J = 10.1, 5.2 Hz, H-1), 3.69 (1H, dt, J = 9.5, 6.8 Hz, -OCH_2-), 3.66–3.82 and 3.98–4.01 (3H, 2 sets of m, H-5′, H-2 or -OCH_2-), 3.81 (1H, dd, J = 9.8, 6.1 Hz, H-6′), 3.86 (1H, dd, J = 9.8, 7.1 Hz, H-6′), 3.93 (1H, dd, J = 10.1, 7.6 Hz, H-1), 4.04 (1H, br t, H-3′), 4.16 (1H, dd, J = 5.5, 1.8 Hz, H-4′), 4.20 (1H, d, J = 7.9 Hz, H-1′), 5.57 (1H, dd, J = 15.1, 8.0 Hz, H-4), 5.63 (1H, dd, J = 8.0, 4.0 Hz, H-3), 5.94 (1H, dt, J = 15.1, 6.9 Hz, H-5), 7.44–7.47, 7.56–7.59 and 8.06–8.08 (5H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930, 2860 (C-H), 2105 (-N_3), 1720 (C=O). Anal. calcd for $C_{55}H_{93}N_3O_{13}Si$: C, 64.99; H, 9.22; N, 4.13. Found: C, 65.30; H, 9.08; N, 4.16.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene 30a. A solution of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene **29a** (0.465 g, 0.45 mmol) in pyridine (15 mL) and water (3 mL) was treated with a stream of hydrogen sulfide for ~10 min. The solution was stirred for 12 h, then hydrogen sulfide was bubbled again for ~10 min. The reaction mixture was stirred for another 12 h. The solvents were evaporated under vacuum and the residue was co-evaporated with toluene (2×). The residue was then dissolved in tetrahydrofuran (15 mL) and an aqueous solution of sodium acetate (50%, 3 mL) was added followed by palmitoyl chloride (184 μL, 0.603 mmol) at 0 °C. The mixture was stirred for 30 min at 22 °C and then diluted with ethyl acetate (~15 mL). The organic layer was separated, washed with 1 M aqueous sodium bicarbonate (~15 mL) and brine (~15 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (20–50% ethyl acetate/hexane) to afford the title compound (0.406 g, 73%) as a beige solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s, -Si(CH_3)$_2$), 0.87–0.90 (15H, m, -Si*t*Bu and 2× -CH_3), 1.24–1.49 and 1.60–1.63 (76H, m, -(CH_2)$_{13}$-, -(CH_2)$_{11}$-, -(CH_2)$_2$-, 2×-O*t*Bu and -C(CH_3)$_2$-), 1.83 and 2.02 (2×2H, 2 qa, -CH_2-CH(CO_2tBu)$_2$ and =CH–CH_2-), 2.20 (2H, m, -NHCOCH_2-), 3.12 (1H, t, J = 7.5 Hz, -CH(CO_2tBu)$_2$), 3.40 (1H, dd, J = 6.3, 3.4 Hz, H-2′), 3.60 (2H, t, J = 6.6 Hz, -OCH_2-), 3.71–3.77, 3.80–3.86 and 4.18–4.21 (3×2H, 3 sets of m, H-1, H-6′, H-4′ and H-5′), 4.02 (1H, dd, J = 6.4, 6.4 Hz, H-3′), 4.49 (1H, m, H-2), 4.80 (1H, d, J = 3.3 Hz, H-1′), 5.53 (1H, dd, J = 15.1, 7.5 Hz, H-4), 5.60 (1H, t, J = 7.3 Hz, H-3), 5.87 (1H, dt, J = 15.1, 6.9 Hz, H-5), 6.11 (1H, d, J = 9.1 Hz, -NH-), 7.43–7.47, 7.55–7.59 and 8.03–8.05 (5H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3440 (N–H), 3050, 2980, 2930, 2860 (C–H), 1720, 1675 (C=O). Anal. calcd for $C_{71}H_{125}NO_{13}Si$: C, 69.40; H, 10.25; N, 1.14. Found: C, 69.40; H, 10.13; N, 1.27.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-4-octadecene 33a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene **30a** (0.376 g, 0.30 mmol) was treated with 90% aqueous trifluoroacetic acid (4 mL) at 5 °C. This mixture was stirred for 5 min at 5 °C and then the ice-bath was removed and this was stirred for 10 min. Toluene was added and the mixture was evaporated under vaccuo and coevaporated with toluene (2×). This was repeated until there was no starting material left. The residue was dried in vaccuo, dissolved in chloroform and filtered on Millex LCR carthridge. The solution was triturated with acetonitrile. The residue was recrystallized form chloroform/acetonitrile to give the title compound (0.175 g, 61%) as a white solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.21–1.40, 1.72–1.78 and 1.84–1.89 (52H, 3 sets of m, -(CH_2)$_{13}$-, -(CH_2)$_{11}$- and -(CH_2)$_2$-), 2.02 and 2.33 (2×2H, 2 ap q, -CH_2-CH(CO_2H)$_2$ and =CH–CH_2-), 2.51 (2H, t, J = 7.4 Hz, -NHCOCH_2-), 3.66 (1H, m, -OCH_2-), 3.78 (1H, m, -OCH_2-), 3.83 (1H, t, J = 7.3 Hz, -CH(CO_2H)$_2$), 4.18–4.22, 4.37–4.42 and 4.43–4.50 (2H and 6H, H-1, H-6′, H-5′, H-4′, H-3′ and H-2′), 5.20 (1H, m, H-2), 5.44 (1H, d, J = 3.5 Hz, H-1′), 5.92 (1H, dd, J = 15.4, 7.4 Hz, H-4), 6.09 (1H, dt, J = 15.4, 6.7 Hz, H-5), 6.25 (1H, br t, H-3), 7.41–7.51 and 8.25–8.27 (5H, 2 sets of m, aromatic H), 8.79 (1H, d, J = 8.9 Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}) 3700–3100 (N–H, O–H), 2930, 2860 (C–H), 1720, 1645 (C=O). MS (ESI-): 960.6 (M−H)-. MS (ESI$^+$): 962.7 (MH$^+$), 984.6 (M + Na)$^+$.

Preparation of the sodium salt of the title compound: The diacid from the above procedure (0.159 g, 0.170 mmol) was dissolved in dioxane (10 mL) and fil-

tered on Millex LCR 0.5 m. This solution was treated with an aqueous solution of sodium bicarbonate (30 mg, 0.348 mmol in 5 mL of water). The resulting suspension was then diluted with water to get a slightly cloudy solution which was lyophilized to give the sodium salt of the title compound (0.172 g, 100%) as a white fluffy solid. ^{1}H NMR (400 MHz, CD_3OD) δ 0.83 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.19–1.38, 1.55, 1.77 (48H, 4H and 2H, 3 sets of m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-, -$(CH_2)_2$- and -CH_2-CH($CO_2Na)_2$), 2.00 (2H, dt, J = 6.9, 6.9 Hz, =CH-CH_2-), 2.15 (2H, t, -NHCOCH_2-), 3.03 (1H, t, J = 7.2 Hz, -CH($CO_2Na)_2$), 3.44 (1H, m, -OCH_2-), 3.50 (1H, dd, J = 9.9, 3.6 Hz, H-2′), 3.56–3.65 and 3.73–3.76 (4H and 2H, 2 sets of m, H-1, H-6′, -OCH_2- and H-3′), 3.69 (1H, t, J = 6.0 Hz, H-5′), 3.80 (1H, d, J = 3.1 Hz, H-4′), 4.36 (1H, m, H-2), 4.85 (1H, d, J = 3.5 Hz, H-1′), 5.45 (1H, dd, J = 15.0 and 7.9 Hz, H-4), 5.52 (1H, br t, H-3), 5.84 (1H, dt, J = 15.0 and 6.9 Hz, H-5), 7.40–7.44, 7.52–7.56 and 7.95–7.97 (5H, 3 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}): 3700–3100 (N–H, O–H), 2920, 2850 (C–H), 1710, 1645, 1585 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-carboxypentyl)-β-D-galactopyranosyloxy]-4-octadecene 33b

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyloxy]-4-octadecene 30b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyloxy]-4-octadecene **29b** (0.473 g, 0.465 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.396 g, 69%) as a slighlty yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 and 0.05 (6H, 2 s, -Si$(CH_3)_2$), 0.88–0.91 (15H, m, -Si*t*Bu and 2×-CH_3), 1.32 and 1.51 (2×3H, 2 s, -C$(CH_3)_2$-), 1.24–1.39 and 1.47–1.67 (52H, 2 sets of m, -$(CH_2)_2$-, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.47 (18H, s, 2×-O*t*Bu), 1.80 (2H, dt, J = 7.8, 7.8 Hz, -CH_2-CH(CO_2tBu)$_2$), 2.02 (2H, dt, J = 7.0, 7.0 Hz, =CH-CH_2-), 2.15 (2H, m, -NHCOCH_2-), 3.11 (1H, t, J = 7.5 Hz, -CH(CO_2tBu)$_2$), 3.24 (1H, br dd, H-2′), 3.58–3.77 and 4.15–4.18 (5H and 1H, 2 sets of m, -OCH_2-, H-6, H-5′ and H-1), 3.81 (1H, dd, J = 9.5, 7.3 Hz, H-1 or H-6′), 4.04 (1H, dd, J = 5.7, 6.5 Hz, H-3′), 4.16 (1H, dd, J = 5.7, 1.4 Hz, H-4′), 4.17 (1H, d, J = 7.8 Hz, H-1′), 4.46 (1H, m, H-2), 5.51 (1H, dd, J = 15.1, 7.4 Hz, H-4), 5.58 (1H, br t, H-3), 5.86 (1H, dt, J = 15.1, 6.9 Hz, H-5), 6.29 (1H, d, J = 9.1 Hz, -NH-), 7.42–7.45, 7.54–7.57 and 8.03–8.06 (5H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3690 (N-H), 3050, 2980, 2930, 2860 (C–H), 1720, 1670 (C=O). Anal. calcd for $C_{71}H_{125}NO_{13}Si$: C, 69.40; H, 10.25; N, 1.14. Found: C, 69.70; H, 10.31; N, 1.24.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-carboxypentyl)-β-D-galactopyranosyloxy]-4-octadecene 33b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyloxy]-4-octadecene **30b** (0.358 g, 0.29 mmol) was reacted by the procedure used to synthesize compound 33a and afforded the title compound (0.217 g, 78%) as a white solid. Diacid: ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.23–1.44 and 1.79–1.91 (52H, 2 sets of m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$- and -$(CH_2)_2$-), 2.04 (2H, dt, J = 6.9, 6.9 Hz, =CH-CH_2-), 2.40 (2H, ap q, -CH_2-CH($CO_2H)_2$), 2.48 (2H, t, J = 7.4 Hz, -NHCOCH_2-), 3.90 (1H, t, J = 7.4 Hz, -CH($CO_2H)_2$), 3.92–4.07 (4H, m, H-2′, H-3′, H-5′ and -OCH_2-), 4.17–4.24 (1H, m, -OCH_2-), 4.23 (1H, dd, J = 10.6, 5.1 Hz, H-1), 4.34 (1H, dd, J = 10.9, 6.0 Hz, H-6′), 4.40 (1H, dd, J = 10.9, 6.0 Hz, H-6′), 4.48 (1H, dd, J = 10.6, 6.3 Hz, H-1), 4.49 (1H, br s, H-4′), 4.79 (1H, d, J = 7.0 Hz, H-1′), 5.20 (1H, m, H-2), 5.93 (1H, dd, J = 15.4, 7.4 Hz, H-4), 6.11 (1H, dt, J = 15.4, 6.7 Hz, H-5), 6.26 (1H, br t, H-3), 7.36–7.40, 7.45–7.55 and 8.23–8.25 (5H, 3 sets of m, aromatic H), 8.52 (1H, d, J = 8.7 Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}) 3700–2400 (O–H, N–H), 2920, 2850 (C–H), 1710, 1640 (C=O). MS (ESI$^-$): 960.6 (M−H)$^-$. MS (ESI$^+$): 962.6 (MH$^+$), 984.6 (M + Na)$^+$. Sodium salt: ^{1}H NMR (400 MHz, CD_3OD) δ 0.89 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.25–1.53, 1.59–1.64 and 1.7–1.9 (54H, 3 sets of m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-, -CH_2-CH($CO_2Na)_2$ and -$(CH_2)_2$-), 2.08 (2H, dt, J = 6.9, 6.9 Hz, =CH–CH_2-), 2.20 (2H, m, -NHCOCH_2-), 3.09 (1H, t, J = 6.8 Hz, -CH($CO_2Na)_2$), 3.31–3.29 (1H, m, H-2′), 3.43 (1H, dd, J = 6.0, 6.0 Hz, H-5′), 3.48 (1H, dd, J = 9.5, 3.3 Hz, H-3′), 3.64–3.66 (3H, m, -OCH_2- and H-6′), 3.76 (1H, dd, J = 10.6, 5.3 Hz, H-1), 3.80 (1H, d, J = 3.2 Hz, H-4′), 3.79–3.86 (1H, m, -OCH_2-), 3.96 (1H, dd, J = 10.6, 6.3 Hz, H-1), 4.25 (1H, d, J = 7.7 Hz, H-1′), 4.47 (1H, m, H-2), 5.55 (1H, dd, J = 15.2, 7.7 Hz, H-4), 5.63 (1H, dd, J = 7.5, 6.0 Hz, H-3), 5.89 (1H, dt, J = 15.2, 6.9 Hz, H-5), 7.44–7.48, 7.57–7.61 and 8.00–8.02 (5H, 3 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3700-2500 (O–H, N–H), 2920, 2850 (C–H), 1710, 1640, 1575 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-carboxypropyl)-α-D-galactopyranosyloxy]-4-octadecene 34a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene 31a and (2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyloxy]-4-octadecene 31b. Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside **12** (0.81 g, 1.30 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-benzoyloxy-4-octadecen-1-ol **28** (0.375 g, 0.87 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** except that dioxane was used as solvent. This afforded the α-anomer (0.155 g, 18%) and the β-anomer (0.050 g, 6%) of the title compound as oils. **α-Anomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (6H, m, -Si$(CH_3)_2$), 0.89 (3H, t overlapped by -Si*t*Bu, -CH_3), 0.91 (9H, s, -Si*t*Bu), 0.92–1.40 (22H, m, -$(CH_2)_{11}$-), 1.33 (3H, s, -C$(CH_3)_2$), 1.45 (18H, s, 2×-O*t*Bu), 1.50 (3H, s, -C$(CH_3)_2$), 2.05–2.09 (4H, m, =CH-CH_2- and -CH_2-CH(CO_2tBu)$_2$), 3.43–3.47 (2H, m, -CH(CO_2tBu)$_2$ and H-2), 3.53 (1H, dd, J = 10.7, 8.0 Hz, H-1), 3.63 (1H, dt, J = 9.8, 6.0 Hz, -OCH_2-), 3.72 (1H, dt, J = 9.8, 6.0 Hz, -OCH_2-), 3.78 (1H, dd, J = 10.0, 6.6 Hz, H-6′), 3.84–3.88, 4.00–4.05 and 4.21–4.27 (3×1H, 3 sets of m, H-1,

H-5′ and H-6′), 3.85 (1H, dd, $J=6.5$, 3.3 Hz, H-2′), 4.03 (1H, dd, $J=6.5$, 2.2 Hz, H-3′), 4.22 (1H, dd, $J=5.6$, 2.2 Hz, H-4′), 4.91 (1H, d, $J=3.4$ Hz, H-1′), 5.55–5.60 (2H, m, H-3 and H-4), 5.93 (1H, br dt, H-5), 7.44–7.48, 7.56–7.60 and 8.06–8.08 (5H, 3 sets of m, aromatic H). **β-Anomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s, -Si$(CH_3)_2$), 0.89 (12H, m, -Si*t*Bu and -CH_3), 1.24 (20H, m, -$(CH_2)_{10}$-), 1.31 (3H, s, -C$(CH_3)_2$), 1.34–1.50 (2H, m, -CH_2-), 1.44 and 1.45 (18H, 2 s , 2×-O*t*Bu), 1.51 (3H, s, -C$(CH_3)_2$), 2.04–2.14 (4H, m, =CH-CH_2- and -CH_2-CH$(CO_2t$Bu$)_2$), 3.24 (1H, t, $J=7.3$ Hz, -CH$(CO_2t$Bu$)_2$), 3.42 (1H, br dd, H-2′), 3.61 (1H, dd, $J=10.3$, 5.0 Hz, H-1), 3.70–3.76 (2H, m, H-2 and -OCH_2-), 3.78–3.93 (1H, m, -OCH_2-), 3.80 (1H, dd, $J=10.0$, 5.8 Hz, H-6′), 3.86 (1H, dd, $J=10.0$, 7.2 Hz, H-6′), 3.90 (1H, dd, $J=10.2$, 7.7 Hz, H-1), 4.01–4.06 (2H, m, H-3′ and H-5′), 4.16 (1H, dd, $J=5.6$, 1.8 Hz, H-4′), 4.20 (1H, d, $J=7.8$ Hz, H-1′), 5.56 (1H, dd, $J=14.8$, 8.0 Hz, H-4), 5.62 (1H, dd, $J=8.0$, 4.0 Hz, H-3), 5.93 (1H, dt, $J=14.8$, 6.7 Hz, H-5), 7.42–7.46, 7.55–7.58 and 8.05–8.07 (5H, 3 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene 32a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene **31a** (0.230 g, 0.233 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.168 g, 60%) as an oil. $[\alpha]_D^{22}$ +40° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s, -Si$(CH_3)_2$), 0.90 (15H, m, -Si*t*Bu and 2×-CH_3), 1.25–1.27 (46H, m, -$(CH_2)_{10}$ and -$(CH_2)_{13}$-), 1.31 (3H, s, -C$(CH_3)_2$), 1.43 and 1.45 (18H, 2 s, -O*t*Bu), 1.46 (3H, s, -C$(CH_3)_2$), 1.49–1.62 (4H, m, -CH_2- and -CH_2-CH$(CO_2t$Bu$)_2$), 2.00–2.09 and 2.13–2.22 (2×2H, 2 sets of m, -NHCOCH_2- and =CH–CH_2-), 3.40 (1H, dd, $J=6.3$, 3.3 Hz, H-2′), 3.46 (1H, t, $J=7.5$ Hz, -CH$(CO_2t$Bu$)_2$), 3.57–3.70 (3H, m, -OCH_2- and H-1), 3.74 (1H, dd, $J=9.8$, 6.3 Hz, H-6′), 3.83 (1H, dd, $J=9.8$, 7.1 Hz, H-6′), 3.88 (1H, dd, $J=10.6$, 3.6 Hz, H-1), 4.00 (1H, br dd, H-5′), 4.18–4.21 (2H, m, H-3′ and H-4′), 4.49 (1H, m, H-2), 4.79 (1H, d, $J=3.2$ Hz, H-1′), 5.54 (1H, dd, $J=15.3$, 7.5 Hz, H-4), 5.65 (1H, br t, H-3), 5.89 (1H, dt, $J=15.3$, 6.7 Hz, H-5), 6.59 (1H, d, $J=8.8$ Hz, -NH-), 7.42–7.46, 7.53–7.58 and 8.03–8.05 (5H, 3 sets of m, aromatic H). IR (film) ν_{max} (cm^{-1}) 3290 (NH), 2920, 2850 (C-H), 1740, 1715, 1640 (C=O). Anal. calcd for $C_{69}H_{121}NO_{13}Si$: C, 69.02; H, 10.16; N, 1.17. Found: C, 69.05; H, 10.12; N, 1.23.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-carboxypropyl)-α-D-galactopyranosyloxy]-4-octadecene 34a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-galactopyranosyloxy]-4-octadecene **32a** (0.155 g, 0.129 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.081 g, 67%) as a beige solid. Diacid: ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, $J=6.7$ Hz, 2×-CH_3), 1.23–1.39 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.81–1.90 and 2.00 (2×2H, 2 sets of m, -CH_2-CH$(CO_2H)_2$ and -CH_2-), 2.53 (2H, t, $J=7.4$ Hz, -NHCOCH_2-), 2.76 (2H, dt, $J=6.6$, 6.6 Hz, =CH–CH_2-), 4.07 (1H, dt, $J=9.3$, 6.2 Hz, -OCH_2-), 4.16 (1H, dt, $J=9.3$, 6.0 Hz, -OCH_2-), 4.23 (1H, dd, $J=10.7$, 6.6 Hz, H-6′), 4.28–4.35 and 4.43–4.55 (7H, 2 sets of m, H-1, H-2′, H-3′, H-4′, H-6′, H-5′ and -CH$(CO_2H)_2$), 4.38 (1H, dd, $J=10.4$, 4.8 Hz, H-1), 5.17–5.22 (1H, m, H-2), 3.52 (1H, d, $J=3.5$ Hz, H-1′), 5.92 (1H, dd, $J=15.4$, 7.3 Hz, H-4), 6.08 (1H, dt, $J=15.4$, 6.6 Hz, H-5), 6.29 (1H, br t, H-3), 7.36–7.40, 7.45–7.49 and 8.24–8.28 (5H, 3 sets of m, aromatic H), 8.80 (1H, d, $J=8.6$ Hz, -NH-). Sodium salt: ^{1}H NMR (400 MHz, CD_3OD) δ 0.83 (6H, m, 2×-CH_3), 1.21–1.39 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$), 1.53 (2H, m, -CH_2-), 1.98–2.19 (6H, m, -NHCOCH_2-, =CH-CH_2- and -CH_2-CH$(CO_2Na)_2$), 5.21 (1H, t, $J=6.9$ Hz, -CH$(CO_2Na)_2$), 3.46–3.80 (10H, m, H-1, H-2′, H-3′, H-4′, H-5′, H-6′ and -OCH_2-), 4.35 (1H, m, H-2), 4.88 (1H, d, $J=2.5$ Hz, H-1′), 5.46 (1H, dd, $J=14.8$, 8.0 Hz, H-4), 5.53 (1H, br t, H-3), 5.84 (1H, dt, $J=14.8$, 6.4 Hz, H-5), 7.39–7.43, 7.51–7.55 and 7.96–7.98 (5H, 3 sets of m, aromatic H). IR (film) ν_{max} (cm^{-1}) 3700–3000 (NH), 2920, 2850 (C–H), 1720, 1650, 1600 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-dicarboxypentyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 41a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 36a and (2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 36b. Ethyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **18** (0.780 g, 1.12 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-benzoyloxy-4-octadecen-1-ol **28** (0.423 g, 0.99 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** and afforded the α-anomer ot the title compound (0.630 g, 60%) and the β-anomer of the title compound (~300 mg, ~29%) as yellow oils. **α-Anomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, $J=6.8$ Hz, -CH_3), 1.25–1.38 (22H, m, -$(CH_2)_{11}$-), 1.42 (18H, s, 2×-O*t*Bu), 1.42–1.44, 1.51–1.57 and 1.68–1.74 (3×2H, 3m, -$(CH_2)_3$-), 2.09 (2H, dt, $J=6.8$, 6.8 Hz, =CH-CH_2-), 2.96 (1H, t, $J=7.5$ Hz, -CH$(CO_2t$Bu$)_2$), 3.55–3.48 (3H, m, H-1 and -OCH_2-), 3.87 (1H, dd, $J=10.8$, 4.2 Hz, H-1), 3.88 (1H, br s, H-5′), 4.03 (1H, m, H-2), 4.09 (1H, dd, $J=12.5$, 1.2 Hz, H-6′), 4.12 (1H, dd, $J=10.5$, 3.4 Hz, H-2′), 4.29 (1H, dd, $J=12.5$, 0.7 Hz, H-6′), 4.61 (1H, d, $J=3.5$ Hz, H-4′), 5.18 (1H, d, $J=3.4$ Hz, H-1′), 5.45 (1H, dd, $J=10.5$, 3.5 Hz, H-3′), 5.52 (1H, s, -OCHO-), 5.57–5.66 (2H, m, H-3 and H-4), 5.97 (1H, dt, $J=14.4$, 6.8 Hz, H-5), 7.34–7.36, 7.44–7.49, 7.55–7.60 and 8.06–8.08 (15H, 4 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 2920, 2850 (C–H), 1720 (C=O). Anal. calcd for $C_{60}H_{83}N_3O_{13}$: C, 68.35; H, 7.93; N, 3.99. Found: C, 68.19; H, 7.79; N, 4.03. **β-Anomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, $J=6.8$ Hz, -CH_3), 1.12–1.33 (22H, m, -$(CH_2)_{11}$-), 1.38–1.46 (2H, m, -CH_2-), 1.41 and 1.42 (18H, 2s, 2× -O*t*Bu), 1.47–1.60 (2H, m, -CH_2-), 1.62–1.70 (2H, m, -CH_2-), 2.09 (2H, dt, $J=6.9$, 6.9 Hz, =CH-CH_2-), 2.90 (1H, t, $J=7.5$ Hz, -CH$(CO_2t$Bu$)_2$), 3.54 (1H, s, H-

5′), 3.60–3.69 (2H, m, -OCH_2- and H-1), 3.84 (1H, dd, J = 10.1, 7.6 Hz, H-2′), 3.82–3.91 (1H, m, -OCH_2-), 4.02–4.09 (3H, m, H-6′, H-1 and H-2), 4.34 (1H, dd, J = 0.7, 11.9 Hz, H-6′), 4.46–4.48 (2H, m, H-1′ and H-4′), 5.10 (1H, dd, J = 10.1, 3.6 Hz, H-3′), 5.51 (1H, s, -OCHO-), 5.60 (1H, dd, J = 15.0, 8.0 Hz, H-4), 5.67 (1H, dd, J = 8.0, 3.4 Hz, H-3), 5.96 (1H, dt, J = 15.0, 6.9 Hz, H-5), 7.32–7.39, 7.41–7.53, 7.56–7.60 and 8.05–8.13 (15H, 4 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3025, 2980, 2930, 2850 (C-H), 2100 (-N_3), 1720 (C=O). Anal. calcd for $C_{60}H_{83}N_3O_{13}$: C, 68.35; H, 7.93; N, 3.99. Found: C, 68.14; H, 7.92; N, 3.83.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 37a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **36a** (0.620 g, 0.588 mmol) was reacted by the procedure used to synthesize compound **30a** and gave the title compound (0.600 g, 81%) as a beige solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.6 Hz, 2× -CH_3), 1.23–1.30 (48H, br s, -$(CH_2)_{11}$- and -$(CH_2)_{13}$-), 1.42 (18H, s, 2×-O*t*Bu), 1.52–1.74 (6H, m, -$(CH_2)_3$-), 2.03 (2H, dt, J = 7.0, 7.0 Hz, =CH-CH_2), 2.22 (2H, m, NHCOCH_2-), 2.95 (1H, t, J = 7.5 Hz, -$CH(CO_2t$Bu$)_2$), 3.54 (1H, dt, J = 9.2, 6.8 Hz, -OCH_2-), 3.69 (1H, dt, J = 9.2, 6.5 Hz, -OCH_2-), 3.80 (1H, s, H-5′), 3.83 (1H, d, J = 11.1, 4.1 Hz, H-1), 3.88 (1H, d, J = 11.1, 3.4 Hz, H-1), 4.03–4.09 (2H, m, H-6′ and H-2′), 4.25 (1H, d, J = 12.2 Hz, H-6′), 4.50–4.55 (1H, m, H-2), 4.55 (1H, d, J = 3.5 Hz, H-4′), 5.07 (1H, d, J = 3.4 Hz, H-1′), 5.45 (1H, dd, J = 10.5, 3.5 Hz, H-3′), 5.50 (1H, s, -OCHO-), 5.53 (1H, dd, J = 15.1, 7.6 Hz, H-4), 5.60 (1H, t, J = 7.6 Hz, H-3), 3.88 (1H, dt, J = 15.1, 7.0 Hz, H-5), 6.17 (1H, d, J = 9.3 Hz, -NH-), 7.33–7.37, 7.42–7.60 and 8.03–8.09 (15H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3300 (NH), 2920, 2850 (C–H), 1720, 1675 (C=O).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 40a. A stirred solution of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **37a** (0.225 g, 0.178 mmol) in methylene chloride (10 mL) was treated at 0 °C with aqueous trifluoroacetic acid (90%, 1 mL). The solution was stirred at 0 °C for 3 h, then solid sodium bicarbonate followed by anhydrous magnesium sulfate were added. The mixture was filtered and evaporated. The residue was purified by silica gel column chromatography (20–50% ethyl acetate/hexane) and afforded the title material (0.158 g, 75%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2× -CH_3), 1.24–1.33 (48H, m, -$(CH_2)_{11}$- and -$(CH_2)_{13}$-), 1.43 (18H, 2s, 2×-O*t*Bu), 1.51–1.74 (6H, m, -$(CH_2)_3$-), 1.99–2.06 (2H, m, =CH-CH_2-), 2.22 (2H, m, -NHCOCH_2-), 2.50 (1H, t, J = 6.2 Hz, -OH-6′), 2.63 (1H, d, J = 3.0 Hz, -OH-4′), 2.94 (1H, t, J = 7.5 Hz, -CH-$(CO_2t$Bu$)_2$), 3.52 (1H, dt, J = 9.3, 6.8 Hz, -OCH_2-), 3.69 (1H, dt, J = 9.3 and 6.4 Hz, -OCH_2-), 3.83–3.93 (5H, m, H-1, H-3′ and H-6′), 3.99 (1H, dd, J = 10.4, 3.6 Hz, H-2′), 4.34 (1H, br s, H-4′), 4.58 (1H, m, H-2), 5.07 (1H, d, J = 3.6 Hz, H-1′), 5.38 (1H, dd, J = 10.4, 3.1 Hz, H-3′), 5.53 (1H, dd, J = 15.0, 7.5 Hz, H-4), 5.59 (1H, t, H-3), 5.89 (1H, dt, J = 15.0, 6.8 Hz, H-5), 6.18 (1H, d, J = 9.4 Hz, -NH-), 7.44–7.50, 7.56–7.62 and 8.03–8.09 (10H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3650–3100 (OH and NH), 2920, 2850 (C–H), 1720, 1650 (C=O). Anal. calcd for $C_{69}H_{111}NO_{14}$: C, 70.32; H, 9.49; N, 1.19. Found: C, 70.27; H, 9.42; N, 1.19.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-dicarboxypentyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 41a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene **40a** (0.173 g, 0.147 mmol) was reacted by the procedure used to synthesize compound **33a** and gave the title compound (0.082 g, 52%) as a white solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, J = 6.6 Hz, 2×-CH_3), 1.24–1.41 (48H, m, -$(CH_2)_{11}$- and -$(CH_2)_{13}$-), 1.68–1.77 (2H, m, -(CH_2)-), 1.88, 2.05 and 2.30 (3×2H, 3m, -$(CH_2)_2$- and =CH-CH_2-), 2.51 (2H, t, J = 7.3 Hz, -NHCOCH_2-), 3.69–3.71 (1H, m, -OCH_2-), 3.78 (1H, t, J = 7.4 Hz, -$CH(CO_2H)_2$), 3.83–3.87 (1H, m, -OCH_2-), 4.26 (1H, dd, J = 10.8, 5.9 Hz, H-6′), 4.38–4.46 (3H, m, H-1 and H-6′), 4.59 (1H, dd, J = 6.0, 6.0 Hz, H-5′), 4.64 (1H, dd, J = 10.5, 3.4 Hz, H-2′), 4.97 (1H, d, J = 2.7 Hz, H-4′), 5.21 (1H, m, H-2), 5.57 (1H, d, J = 3.4 Hz, H-1′), 5.91–5.97 (2H, m, H-3′ and H-4), 6.10 (1H, dt, J = 15.4, 6.7 Hz, H-5), 6.28 (1H, t, J = 6.8 Hz, H-3), 7.38–7.51 and 8.23–8.28 (10H, 2 sets of m, aromatic H), 8.95 (1H, d, J = 8.7 Hz, -NH-). IR (KBr) ν_{max} (cm^{-1}): 3700–3100 (OH and NH), 2920, 2850 (C–H), 1720, 1650 (C=O). MS (ESI^+): 1088.9 $(M+Na)^+$. MS (ESI^-): 1064.8 $(M-H)^-$.

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-carboxypentyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 41b

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 37b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **36b** (0.371 g, 0.35 mmol) was reacted by the procedure used to synthesize compound **30a** and gave the title compound (0.364 g, 82%) as a beige solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, m, 2×-CH_3), 1.14–1.36 (48H, m, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.41 and 1.42 (18H, 2 s, 2× -O*t*Bu), 1.41–1.51 and 1.58–1.67 (6H, 2 sets of m, -CH_2-CH$(CO_2t$Bu$)_2$ and -$(CH_2)_2$-), 2.03 (2H, q, J = 7.0 Hz, =CH-CH_2-), 2.15 (2H, m, -NHCOCH_2-), 2.87 (1H, t, J = 7.5 Hz, -$CH(CO_2t$Bu$)_2$), 3.54 (1H, br s, H-5′), 3.59 (1H, dt, J = 9.4, 6.9 Hz, -OCH_2-), 3.75–3.86 (3H, m, -OCH_2-, H-2′ and H-1), 4.06 (1H, d, J = 11.9 Hz, H-6′), 4.16 (1H, dd, J = 11.2, 4.6 Hz, H-1), 4.28 (1H, d, J = 11.9 Hz, H-6′), 4.44 (1H, d, J = 7.9 Hz, H-1′), 4.46 (1H, d, J = 3.8 Hz, H-4′), 4.50 (1H, m, H-2), 5.08 (1H, dd, J = 10.1, 3.8 Hz, H-3′), 5.50 (1H, s, -OCHO-), 5.53 (1H, dd, J = 15.3, 7.4 Hz, H-4), 5.67 (1H, br t, H-3), 5.87 (1H, dt, J = 15.3, 7.0 Hz, H-5), 6.21 (1H,

d, $J=8.8$ Hz, -NH-), 7.34–7.38, 7.42–7.49, 7.54–7.60 and 8.04–8.09 (15H, 4 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3400 (NH), 3050, 2930, 2850 (C-H), 1720, 1670 (C=O). Anal. calcd for $C_{76}H_{115}NO_{14}$: C, 72.06; H, 9.15; N, 1.11. Found: C, 72.09; H, 9.10; N, 1.29.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 40b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **37b** (0.436 g, 0.27 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.259 g, 81%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, $J=6.8$ Hz, 2×-CH_3), 1.19–1.39 (48H, m, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.43 (18H, s, 2×-O*t*Bu), 1.46–1.53 and 1.58–1.73 (2H and 4H, -CH_2-CH$(CO_2tBu)_2$ and -$(CH_2)_2$-), 2.03–2.25 (2H, br s, 2×-OH), 2.05 (2H, dt, $J=6.9$, 6.9 Hz, =CH-CH_2-), 2.19 (2H, m, -NHCOCH_2-), 2.89 (1H, t, $J=7.5$ Hz, -CH-$(CO_2tBu)_2$), 3.43 (1H, br dd, $J=3.4$, 3.4 Hz, H-5′), 3.60 (1H, dt, $J=9.4$, 6.6 Hz, -OCH_2-), 3.67 (1H, dd, $J=12.5$, 3.2 Hz, H-6′), 3.75–3.85 (4H, m, H-2′, H-1, H-6′ and -OCH_2-), 4.01 (1H, dd, $J=10.5$, 2.7 Hz, H-1), 4.27 (1H, d, $J=2.9$ Hz, H-4′), 4.44 (1H, d, $J=7.6$ Hz, H-1′), 4.62 (1H, m, H-2), 4.98 (1H, dd, $J=10.0$, 3.0 Hz, H-3′), 5.55 (1H, dd, $J=15.4$, 7.9 Hz, H-4), 5.77 (1H, t, $J=7.9$ Hz, H-3), 5.86 (1H, d, $J=9.4$ Hz, -NH-), 5.95 (1H, dt, $J=15.4$, 6.9 Hz, H-5), 7.46–7.49, 7.57–7.62 and 8.05–8.10 (10H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3600, 3450–3350 (NH and OH), 3050, 2930, 2850 (C–H), 1720, 1675 (C=O). Anal. calcd for $C_{69}H_{111}NO_{14}$: C, 70.32; H, 9.49; N, 1.19. Found: C, 70.78; H, 9.52; N, 1.30.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-carboxypentyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 41b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene (0.240 g, 0.2 mmol) **40b** was reacted by the procedure used to synthesize compound **33a** and gave the title compound (0.139 g, 65%) as a white solid. **Diacid:** ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, $J=6.7$ Hz, 2×-CH_3), 1.24 (44H, br s, -$(CH_2)_{12}$- and -$(CH_2)_{10}$-), 1.41, 1.67–1.92, 2.04 and 2.24–2.32 (2H, 6H, 2×2H, 4 sets of m, 2×-CH_2-, -$(CH_2)_2$-, -CH_2-CH$(CO_2H)_2$ and =CH-CH_2-), 2.49 (2H, t, $J=7.4$ Hz, -NHCOCH_2-), 3.73 (1H, t, $J=7.4$ Hz, -CH$(CO_2H)_2$), 3.90 (1H, m, -OCH_2-), 4.07 (1H, dd, $J=6.2$, 6.2 Hz, H-5′), 4.19 (1H, m, -OCH_2-), 4.27 (1H, dd, $J=10.4$, 5.2 Hz, H-1), 4.32 (1H, dd, $J=10.9$, 6.1 Hz, H-6′), 4.37–4.43 (2H, m, H-2′ and H-6′), 4.52 (1H, dd, $J=10.4$, 6.7 Hz, H-1), 4.91–4.93 (2H, m, H-1′ and H-4′), 5.25 (1H, m, H-2), 5.57 (1H, dd, $J=10.1$, 3.1 Hz, H-3′), 5.94 (1H, dd, $J=15.4$, 7.3 Hz, H-4), 6.12 (1H, dt, $J=15.4$, 6.7 Hz, H-5), 6.28 (1H, br t, H-3), 7.19–7.50 and 8.24–8.26 (10H, 2 sets of m, aromatic H), 8.60 (1H, d, $J=8.7$ Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}) 3700–3100 (NH and OH), 2930, 2850 (C-H), 1715, 1645 (C=O). MS (ESI^-): 1064.7 $(M-H)^-$. MS (ESI^+): 1066.7 (MH^+), 1088.7 $(M+Na)^+$. Sodium salt: ^{1}H NMR (400 MHz, CD_3OD) δ 0.89 (6H, t, $J=6.8$ Hz, 2×-CH_3), 1.25–1.31 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.40, 1.49, 1.59 and 1.73 (4×2H, 4 sets of m, -CH_2-, -$(CH_2)_2$- and -CH_2-CH$(CO_2Na)_2$), 2.09 (2H, dt, $J=6.9$, 6.9 Hz, =CH-CH_2-), 2.18–2.24 (2H, m, -NHCOCH_2-), 2.97 (1H, br t, -CH$(CO_2Na)_2$), 3.56–3.66 (4H, m, H-5′, H-6′, H-1 and -OCH_2-), 3.69 (1H, dd, $J=10.1$, 7.7 Hz, H-2′), 3.77–3.83 (1H, m, -OCH_2-), 3.84 (1H, dd, $J=10.7$, 5.4 Hz, H-1), 3.99 (1H, dd, $J=10.5$, 6.3 Hz, H-6′), 4.11 (1H, d, $J=3.1$ Hz, H-4′), 4.43 (1H, d, $J=7.7$ Hz, H-1′), 4.51 (1H, m, H-2), 4.94 (1H, dd, $J=10.1$, 3.3 Hz, H-3′), 5.56 (1H, dd, $J=15.2$, 7.7 Hz, H-4), 5.65 (1H, br t, H-3), 5.91 (1H, dt, $J=15.2$, 6.9 Hz, H-5), 7.45–7.51, 7.58–7.61 and 7.99–8.08 (10H, 3 sets of m aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3650–3100 (NH and OH), 2920, 2850 (C–H), 1720, 1650, 1595 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 43a

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 38a and (2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 38b. Ethyl 2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (1.97 g, 3.00 mmol) **20**, 2,6-di-*tert*-butyl-4-methylpyridine (1.23 g, 6.0 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-benzoyloxy-4-octadecen-1-ol **28** were reacted by the procedure used to synthesize compounds **29a** and **b** except that dioxane was used as solvent. This gave the α-anomer (1.64 g, 64%) and the β-anomer (0.51 g, 20%) of the title compound as oils. **α-anomer:** $[\alpha]_D^{22}$ +71.8° (*c* 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, $J=6.8$ Hz, -CH_3), 1.26 (20H, br s, -$(CH_2)_{10}$-), 1.39–1.42 (20H, m, 2×-O*t*Bu and -CH_2-), 2.01–2.12 (4H, m, =CH-CH_2- and -CH_2–CH$(CO_2tBu)_2$), 3.41 (1H, t, $J=7.4$ Hz, -CH$(CO_2tBu)_2$), 3.64–3.72 (3H, m, H-2, H-2′ and -OCH_2-), 3.89 (1H, dd, $J=10.7$, 4.2 Hz, H-1), 3.90 (1H, br s, H-5′), 4.04 (1H, dt, $J=7.8$, 4.0 Hz, -OCH_2-), 4.10 (1H, br d, $J=12.5$ Hz, H-6′), 4.14 (1H, dd overlapped by H-6′, H-1), 4.30 (1H, br d, $J=12.5$ Hz, H-6′), 4.64 (1H, d, $J=3.4$ Hz, H-4′), 5.19 (1H, d, $J=3.4$ Hz, H-1′), 5.45 (1H, dd, $J=10.5$, 3.4 Hz, H-3′), 5.52 (1H, s, -OCHO-), 5.62 (1H, dd, $J=14.3$, 8.0 Hz, H-4), 5.66 (1H, dd, $J=8.0$, 4.1 Hz, H-3), 5.98 (1H, dt, $J=14.3$, 6.8 Hz, H-5), 7.33–7.34, 7.43–7.49, 7.56–7.60 and 8.07–8.13 (15H, 4 sets of m, 3×-C_6H_5). IR (film) ν_{max} (cm^{-1}) 3035, 3010, 2970, 2925, 2855 (C–H), 2100 (N_3), 1722 (C=O). Anal. calcd for $C_{58}H_{79}N_3O_{13}$: C, 67.88; H, 7.76; N, 4.09. Found: C, 67.83; H, 7.64; N, 4.20. **β-Anomer:** $[\alpha]_D^{22}$ +28° (*c* 0.97, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, $J=6.8$ Hz, -CH_3), 1.20–1.50 (22H, m, -$(CH_2)_{11}$-), 1.35 and 1.36 (18H, 2 s, 2×-O*t*Bu), 1.96–2.11 (4H, m, =CH–CH_2- and -CH_2-CH$(CO_2tBu)_2$), 3.28 (1H, t, $J=7.3$ Hz, -CH$(CO_2tBu)_2$), 3.54 (1H, br s, H-5′), 3.69 (1H, dt, $J=9.9$, 6.6 Hz, -OCH_2-), 3.72 (1H, dd, $J=10.2$, 4.6 Hz, H-1), 3.86 (1H, dd, $J=10.1$, 7.7 Hz, H-2′), 3.94 (1H, dt, $J=9.9$, 6.0 Hz, -OCH_2-), 4.02 (1H, dd, $J=10.2$, 7.9 Hz, H-1), 4.07 (1H, d, $J=12.2$ Hz, H-6′), 4.10–4.13 (1H, m, H-2), 4.34 (1H, d, $J=12.2$ Hz, H-6′), 4.47–4.50 (2H, m,

H-1′ and H-4′), 5.07 (1H, dd, $J=10.1$, 3.6 Hz, H-3′), 5.50 (1H, s, -OCHO-), 5.60 (1H, dd, $J=14.4$, 8.0 Hz, H-4), 5.64 (1H, dd, $J=8.0$, 4.0 Hz, H-3), 5.95 (1H, dt, $J=14.4$, 6.7 Hz, H-5), 7.33–7.37, 7.43–7.49, 7.53–7.59 and 8.07–8.13 (15H, 4 sets of m, aromatic H). IR (film) ν_{max} (cm^{-1}) 2930, 2850 (C-H), 2100 (-N_3), 1725 (C=O). Anal. calcd for $C_{58}H_{79}N_3O_{13}$. CH_2Cl_2: C, 63.77; H, 7.35; N, 3.78. Found: C, 64.00; H, 7.35; N, 3.89.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 39a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **38a** (0.477 g, 0.464 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.527 g, 92%) as an oil. $[\alpha]_D^{22}$ +61.5° (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.87–0.91 (6H, m, 2× -CH_3), 1.24–1.44 (44H, m, -$(CH_2)_{10}$- and -$(CH_2)_{12}$-), 1.37 and 1.39 (18H, 2s, 2×-O*t*Bu), 1.53–1.65 (4H, m, 2× -CH_2-), 2.00–2.09 and 2.19–2.40 (6H, 2 sets of m, -NHCOCH_2-, =CH-CH_2- and -CH_2-CH(CO_2tBu)$_2$), 3.39 (1H, t, $J=7.3$ Hz, -CH(CO_2tBu)$_2$), 3.62 (1H, dt, $J=9.5$, 5.8 Hz, -OCH_2-), 3.72–3.82 (2H, m, -OCH_2- and H-1), 3.80 (1H, br s, H-5′), 3.91 (1H, dd, $J=10.9$, 3.4 Hz, H-1), 4.05 (1H, dd, $J=12.4$, 1.3 Hz, H-6′), 4.08 (1H, dd, $J=10.6$, 3.4 Hz, H-2′), 4.25 (1H, d, $J=12.4$ Hz, H-6′), 4.52 (1H, m, H-2), 4.59 (1H, d, $J=3.4$ Hz, H-4′), 5.08 (1H, d, $J=3.4$ Hz, H-1′), 5.39 (1H, dd, $J=10.6$, 3.4 Hz, H-3′), 5.50 (1H, s, -OCHO-), 5.55 (1H, dd, $J=15.3$, 7.5 Hz, H-4), 5.67 (1H, t, $J=7.3$ Hz, H-3), 5.92 (1H, dt, $J=15.3$, 6.8 Hz, H-5), 6.44 (1H, d, $J=9.0$ Hz, -NH-), 7.31–7.33, 7.42–7.48, 7.54–7.60, 8.04–8.12 (15H, 4 sets of m, 3×-C_6H_5). IR (film) ν_{max} (cm^{-1}): 3500–3240 (NH), 2925, 2855 (C–H), 1722, 1650 (C=O). Anal. calcd for $C_{74}H_{111}NO_{14}$: C, 71.75; H, 9.03; N, 1.13. Found: C, 72.02; H, 9.12; N, 1.33.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 42a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **39a** (0.242 g, 0.195 mmol) was reacted by the procedure used to synthesize compound 40a and afforded the title material (0.187 g, 83%) as an oil. $[\alpha]_D^{22}$ +60.1° (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, $J=6.7$ Hz, 2× -CH_3), 1.24–1.47 (62H, m, -$(CH_2)_{10}$-, -$(CH_2)_{12}$- and 2×-O*t*Bu), 1.63 (5H, m, 2×-CH_2- and -OH), 2.00–2.08 (4H, m, =CH–CH_2- and -CH_2–CH(CO_2tBu)$_2$), 2.22 (2H, m, -NHCOCH_2-), 2.65 (1H, br s, -OH), 3.35 (1H, t, $J=7.4$ Hz, -CH(CO_2tBu)$_2$), 3.61 (1H, dt, $J=9.5$, 6.0 Hz, -OCH_2-), 3.73 (1H, dt, $J=9.5$, 6.2 Hz, -OCH_2-), 3.82–3.94 (4H, m, H-1 and H-6′), 3.92 (1H, br s, H-5′), 4.00 (1H, dd, $J=10.5$, 3.6 Hz, H-2′), 4.37 (1H, d, $J=2.9$ Hz, H-4′), 4.56 (1H, m, H-2), 5.07 (1H, d, $J=3.6$ Hz, H-1′), 5.32 (1H, dd, $J=10.5$ and 3.0 Hz, H-3′), 5.54 (1H, dd, $J=15.3$, 7.4 Hz, H-4), 5.64 (1H, t, $J=7.2$ Hz, H-3), 5.91 (1H, dt, $J=15.3$, 6.8 Hz, H-5), 6.38 (1H, d, $J=9.1$ Hz, -NH-), 7.43–7.49, 7.55–7.61 and 8.04–8.11 (10H, 3 sets of m, 3×-C_6H_5). IR (film) ν_{max} (cm^{-1}) 3600–3100 (OH and NH), 2920, 2850 (C–H), 1720, 1650 (C=O).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 43a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene **42a** (0.083 g, 0.072 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.074 g, 98%) as a white fluffy solid. $[\alpha]_D^{22}$ +66° (*c* 0.5, $CHCl_3$). ^1H NMR (400 MHz, DMSO-d_6) δ 0.85 (6H, t, $J=6.8$ Hz, 2×-CH_3), 1.19–1.35 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.47, 1.85, 2.00 and 2.09 (8H, 4 sets of m, -CH_2-, -NHCOCH_2-, =CH-CH_2- and -CH_2CH(CO_2H)$_2$), 3.42 (1H, dd, $J=10.9$ and 6.5 Hz, H-1), 3.47–3.49, 3.51–3.58 and 3.73–3.76 (7H, 3 sets of m, H-5′, H-6′, H-1, -OCH_2- and -CH(CO_2H)$_2$), 3.85 (1H, dd, $J=10.5$, 3.4 Hz, H-2′), 4.10 (1H, br s, H-4′), 4.37 (1H, m, H-2), 4.61 (1H, br s, -OH-6′), 4.97 (1H, d, $J=3.4$ Hz, H-1′), 5.06 (1H, dd, $J=10.5$, 3.0 Hz, H-3′), 5.09 (1H, s, -OH-4′), 5.48 (1H, br t, H-3), 5.55 (1H, dd, $J=15.1$, 7.5 Hz, H-4), 5.7 (1H, dt, $J=15.1$, 6.8 Hz, H-5), 7.47–7.52, 7.61–7.67 and 7.94–8.01 (11H, 3 sets of m, 2× -C_6H_5 and -NH-), 12.63 (1H, br s, -COOH). IR (film) ν_{max} (cm^{-1}) 3700–3000 (OH and NH), 2920, 2850 (C-H), 1720, 1650 (C=O). MS (ESI^-) 1036.6 $(M-H)^-$. MS (ESI^+) 1038.7 (MH^+), 1060.7 $(M+Na)^+$. HRMS (Pos. FAB): calcd for $C_{59}H_{91}O_{14}NNa$: 1060.634711. Found: 1060.63460 δ = −1.0 ppm.

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 43b

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 39b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **38b** (0.467 g, 0.455 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.393 g, 70%) as a clear sticky oil. $[\alpha]_D^{22}$ +36° (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (6H, t, $J=6.7$ Hz, 2×-CH_3), 1.24–1.36 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.39 and 1.41 (18H, 2 s , 2×-O*t*Bu), 1.53–1.60 (2H, m, -CH_2-), 2.00–2.12 (4H, m, -CH_2–CH(CO_2tBu)$_2$ and =CH-CH_2-), 2.21 (2H, t, $J=7.4$ Hz, -NHCOCH_2-), 3.26 (1H, t, $J=7.2$ Hz, -CH(CO_2tBu)$_2$), 3.50 (1H, br s, H-5′), 3.70 (1H, dt, $J=9.6$, 5.9 Hz, -OCH_2-), 3.78 (1H, dd, $J=10.1$, 7.7 Hz, H-2′), 3.76–3.83 (1H, m overlapped by H-2′, -OCH_2-), 3.86 (1H, dd, $J=11.1$, 3.5 Hz, H-1), 4.00 (1H, d, $J=12.2$ Hz, H-6′), 4.16–4.20 (2H, m, H-1 and H-6′), 4.41 (1H, d, $J=7.7$ Hz, H-1′), 4.45 (1H, d, $J=3.6$ Hz, H-4′), 4.52 (1H, m, H-2), 5.04 (1H, dd, $J=10.1$, 3.6 Hz, H-3′), 5.45 (1H, s, -OCHO-), 5.54 (1H, dd, $J=15.5$, 7.5 Hz, H-4), 5.69 (1H, t, $J=7.5$ Hz, H-3), 5.92 (1H, dt, $J=15.5$, 6.7 Hz, H-5), 6.72 (1H, d, $J=8.7$ Hz, -NH-), 7.32–7.60 and 8.04–8.09 (15H, 2 sets of m, aromatic H). IR (film) ν_{max} (cm^{-1}): 2920, 2850 (C-H), 1725, 1680 (C=O). Anal. calcd for $C_{74}H_{111}NO_{14}$: C, 71.75; H, 9.03; N, 1.13. Found: C, 71.77; H, 9.09; N, 1.23.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 43b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **39b** (0.350 g, 0.28 mmol) was treated with anisole (65 μL, 0.56 mmol) followed by 90% aqueous trifluoroacetic acid (6 mL) at 5 °C. This mixture was stirred for 5 min at 5 °C and then the ice-bath was removed and this was stirred for 10 min. Toluene was added and the mixture was evaporated under vaccuo and coevaporated with toluene (2×). This was repeated until there was no starting material left. The residue was dried in vaccuo, dissolved in chloroform and filtered on Millex LCR carthridge. The solution was triturated with acetonitrile. The residue was recrystallized form chloroform/acetonitrile to give the title compound (0.120 g, 41%) as a white solid. **Diacid**: ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.23–1.41 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.87 (2H, m, -CH_2-), 2.03 (2H, m, -CH_2–$CH(CO_2H)_2$), 2.54 (2H, t, J = 7.3 Hz, -NHCOCH_2-), 2.76 (2H, m, =CH-CH_2-), 4.06 (1H, br t, H-5′), 4.20 (1H, t, J = 7.2 Hz, -$CH(CO_2H)_2$), 4.26 (1H, dd, J = 10.5, 5.7 Hz, H-6′), 4.29–4.39 and 4.47–4.57 (3H, m, -OCH_2- and H-1), 4.36 (1H, dd, J = 10.7, 6.7 Hz, H-1), 4.49 (1H, dd, J = 10.0, 7.7 Hz, H-2′), 4.55 (1H, dd, J = 10.5, 6.7 Hz, H-6′), 4.93–4.96 (2H, m, H-1′ and H-4′), 5.25 (1H, m, H-2), 5.55 (1H, dd, J = 10.1, 3.1 Hz, H-3′), 5.94 (1H, dd, J = 15.4, 7.1 Hz, H-4), 6.14 (1H, dt, J = 15.4, 6.7 Hz, H-5), 6.29 (1H, br t, H-3), 7.22–7.40, 7.45–7.49 and 8.23–8.28 (10H, m, aromatic H), 8.59 (1H, d, J = 8.6 Hz, -NH-). Anal. calcd for $C_{59}H_{91}NO_{14}.H_2O$: C, 67.08; H, 8.87; N, 1.33. Found: C, 67.02; H, 8.75; N, 1.83. **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 0.82 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.19–1.32 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.52 (2H, m, -CH_2-), 2.00 and 2.20 (4H and 2H, 2 sets of m, -NHCOCH_2-, =CH-CH_2- and -CH_2-$CH(CO_2Na)_2$), 3.04 (1H, t, J = 7.0 Hz, -$CH(CO_2Na)_2$), 3.45–3.51, 3.63–3.70 and 3.76–3.82 (3H, 2H and 1H, 3 sets of m, -OCH_2- , H-2′, H-5′, H-6′ and H-1), 3.77 (1H, dd, J = 10.7, 4.1 Hz, H-1), 3.99 (1H, dd, J = 10.4, 6.2 Hz, H-6′), 4.04 (1H, br d, H-4′), 4.34 (1H, d, J = 7.6 Hz, H-1′), 4.41 (1H, m, H-2), 4.82 (1H, dd, J = 10.2, 3.4 Hz, H-3′), 5.50 (1H, dd, J = 15.3, 7.2 Hz, H-4), 5.61 (1H, t, J = 7.2 Hz, H-3), 5.85 (1H, dt, J = 15.3, 7.6 Hz, H-5), 7.39–7.43, 7.49–7.54 and 7.95–8.02 (10H, m, aromatic H). IR (KBr) ν_{max} (cm^{-1}) 3700–3100 (O–H), 2920, 2850 (C–H), 1715, 1650, 1600 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-2-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 52a

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 44a and (2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 44b. Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **26** (1.185 g, 1.68 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-benzoyloxy-4-octadecen-1-ol **28** (0.540 g, 1.68 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** except that acetonitrile was used as solvent. This afforded the α-anomer (0.694 g, 39%) and the β-anomer (0.453 g, 25%) of the title compound as yellow oils. **α-Anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.8 Hz, -CH_3), 1.26 (20H, m, -$(CH_2)_{10}$-), 1.36–1.59 (4H, m, -$(CH_2)_2$-), 1.45 and 1.45 (18H, 2 s, 2×-O*t*Bu), 1.67 and 1.83 (2×2H, 2 sets of m, -$(CH_2)_2$-), 2.08 (2H, q, J = 6.9 Hz, =CH-CH_2-), 3.10 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.56–3.76 (5H, m, -OCH_2-, H-1 and H-2), 3.79 (3H, s, -OCH_3), 3.83 (1H, dd, J = 10.2, 3.1 Hz, H-3′), 3.96 (1H, dd, J = 10.2, 3.5 Hz, H-2′), 3.94–3.99 (1H, m overlapped by H-2′, H-5′), 4.07 (1H, dd, J = 12.3, 1.2 Hz, H-6′), 4.23 (1H, d, J = 12.3 Hz, H-6′), 4.33 (1H, d, J = 3.1 Hz, H-4′), 4.56 (1H, d, J = 11.6 Hz, -OCH_2Ar), 4.75 (1H, d, J = 11.6 Hz, -OCH_2Ar), 4.85 (1H, d, J = 3.5 Hz, H-1′), 5.55 (1H, s, -OCHO-), 5.55–5.64 (1H, m overlapped by H-3, H-4), 5.63 (1H, dd, J = 7.9, 4.0 Hz, H-3), 5.93 (1H, dt, J = 14.5, 6.9 Hz, H-5), 6.82–6.85, 7.17–7.39, 7.45–7.53, 7.58–7.62 and 8.06–8.08 (14H, 5 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930 and 2860 (C-H), 1720 (C=O). Anal. calcd for $C_{61}H_{87}N_3O_{13}$: C, 68.45; H, 8.19; N, 3.93. Found: C, 68.46; H, 8.03; N, 3.94. **β-anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.8 Hz, -CH_3), 1.24–1.42 (20H, m, -$(CH_2)_{10}$-), 1.42–1.61 (4H, m, -$(CH_2)_2$-), 1.45 and 1.45 (18H, 2 s, 2×-O*t*Bu), 1.67 and 1.82 (2×2H, 2 sets of m, -$(CH_2)_2$-), 2.04 (2H, m, =CH–CH_2-), 3.09 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.38 (1H, br s, H-5′), 3.43 (1H, dd, J = 9.7, 3.5 Hz, H-3′), 3.57–3.63 (2H, m, -OCH_2- and H-2), 3.69 (1H, dt, J = 9.1, 6.7 Hz, -OCH_2-), 3.77 (1H, dd, J = 9.6, 7.7 Hz, H-2′), 3.79 (3H, s, -OCH_3), 3.99–4.08 (3H, m, H-1 and H-6′), 4.25 (1H, d, J = 3.5 Hz, H-4′), 4.32 (1H, dd, J = 12.3, 0.9 Hz, H-6′), 4.40 (1H, d, J = 7.7 Hz, H-1′), 4.73 (1H, d, J = 10.4 Hz, -OCH_2Ar), 4.82 (1H, d, J = 10.4 Hz, -OCH_2Ar), 5.55 (1H, s, -OCHO-), 5.58 (1H, dd, J = 15.3, 7.9 Hz, H-4), 5.71 (1H, dd, J = 8.0, 3.6 Hz, H-3), 5.90 (1H, dt, J = 15.3, 6.8 Hz, H-5), 6.82–6.90, 7.01–7.60 and 8.07–8.10 (14H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930 and 2850 (C–H), 1720 (C=O). Anal. calcd for $C_{61}H_{87}N_3O_{13}$: C, 68.45; H, 8.19; N, 3.93. Found: C, 68.57; H, 8.03; N, 3.92.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 45a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **44a** (0.718 g, 0.67 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.710 g, 83%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.24–1.27 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.42–1.45 (2H, m, -CH_2-), 1.45 (18H, 2 s, 2×-O*t*Bu), 1.5–1.62 (2H, m, -CH_2-), 1.68, 1.85, 2.00 and 2.09 (4×2H, 4 sets of m, -NHCOCH_2-, =CH–CH_2- and -$(CH_2)_2$-), 3.10 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.57 (1H, dt, J = 9.0, 6.7 Hz, -OCH_2-), 3.64–3.69 (1H, m, -OCH_2-), 3.69 (1H,

br s, H-5′), 3.76–3.83 (3H, m, H-1 and H-2′), 3.78 (3H, s, -OCH_3), 3.95 (1H, dd, J = 10.1, 3.5 Hz, H-3′), 4.05 (1H, d, J = 11.7 Hz, H-6′), 4.21 (1H, d, J = 11.7 Hz, H-6′), 4.31 (1H, br d, H-4′), 4.48 (1H, m, H-2), 4.62 (1H, d, J = 11.1 Hz, -OCH_2Ar), 4.72 (1H, d, J = 11.1 Hz, -OCH_2Ar), 4.88 (1H, d, J = 3.5 Hz, H-1′), 5.48 (1H, dd, J = 15.3, 7.6 Hz, H-4), 5.54 (1H, s, -OCHO-), 5.59 (1H, t, J = 7.4 Hz, H-3), 5.79 (1H, dt, J = 15.3, 6.7 Hz, H-5), 5.99 (1H, d, J = 9.1 Hz, -NH-), 6.81–6.83, 7.30–7.38, 7.45–7.53, 7.57–7.61 and 8.04–8.06 (14H, 5 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3440 (NH), 3050, 2990, 2930 and 2860 (C–H), 1720, 1670 (C=O). Anal. calcd for $C_{77}H_{119}NO_{14}$: C, 72.10; H, 9.35; N, 1.09. Found: C, 72.19; H, 9.31; N, 1.23.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene 48a. A solution of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **45a** (0.675 g, 0.53 mmol) in dichloromethane (12 mL) and water (1.5 mL) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (180 mg, 0.796 mmol) at 5 °C. The mixture was vigorously stirred at 5 °C for 30 min and then at 23 °C for 1 h. The mixture was diluted with dichloromethane (100 mL) and washed with saturated sodium bicarbonate, 10% aqueous sodium thiosulfate (1:1) (60 mL), 10% aqueous sodium thiosulfate (60 mL) and brine (60 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by silica gel chromatography (30–50% ethyl acetate/hexane) and afforded the title compound (0.549 g, 90%) as a beige amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.26 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.40–1.52 (2H, m, -CH_2-), 1.45 and 1.46 (18H, 2 s, 2×-O*t*Bu), 1.59–1.70 (4H, m, -$(CH_2)_2$-), 1.83 and 2.20 (2×2H, 2 sets of m, -NHCOCH_2- and -CH_2-$CH(CO_2tBu)_2$), 2.05 (2H, dt J = 6.9, 6.9 Hz, = CH-CH_2-), 2.50 (1H, br s, -OH), 3.11 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.54 (1H, dt, J = 9.0, 6.6 Hz, -OCH_2-), 3.62 (1H, dd, J = 10.1 3.3 Hz, H-3′), 3.69 (1H, dt, J = 9.0, 6.6 Hz, -OCH_2-), 3.74 (1H, br s, H-5′), 3.76 (1H, dd, J = 11.0, 6.1 Hz, H-1), 3.93 (1H, dd, J = 11.0, 3.8 Hz, H-1), 4.06–4.13 (1H, m, H-2′), 4.08 (1H, dd, J = 12.4, 1.2 Hz, H-6′), 4.26 (1H, dd, J = 12.4, 1.0 Hz, H-6′), 4.32 (1H, br d, H-4′), 4.55 (1H, m, H-2), 4.99 (1H, d, J = 3.7 Hz, H-1′), 5.53 (1H, dd, J = 15.3, 7.4 Hz, H-4), 5.54 (1H, s, -OCHO-), 5.63 (1H, br t, H-3), 5.88 (1H, dt, J = 15.3, 6.9 Hz, H-5), 5.90 (1H, d, J = 9.3 Hz, -NH-), 7.30–7.38, 7.45–7.58, 7.58–7.62 and 8.03–8.05 (10H, m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3700, 3600 3440 (NH and OH), 3050, 2980, 2930 and 2860 (C-H), 1720, 1675 (C=O). Anal. calcd for $C_{69}H_{111}NO_{13}$: C, 71.28; H, 9.62; N, 1.20. Found: C, 71.21; H, 9.52; N, 1.34.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-2-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 50a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **48a** (0.260 g, 0.22 mmol) was reacted by the procedure used to synthesize compound **18** and afforded the title compound (0.262 g, 95%) as a white gummy solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, m, 2×-CH_3), 1.25–1.38 (48H, m, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.42 and 1.43 (18H, 2 s, 2×-O*t*Bu), 1.54–1.63 (4H, m, -$(CH_2)_2$-), 1.74 (2H, m, -CH_2-$CH(CO_2tBu)_2$), 2.02 (4H, m, -NHCOCH_2- and =CH-CH_2-), 2.97 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.55 (1H, dt, J = 9.2, 6.6 Hz, -OCH_2-), 3.65–3.70 (2H, m, -OCH_2- and H-1), 3.81 (1H, s, H-5′), 3.86 (1H, dd, J = 11.0, 4.0 Hz, H-1), 3.99 (1H, dd, J = 10.5, 3.4 Hz, H-3′), 4.11 (1H, d, J = 12.5 Hz, H-6′), 4.30 (1H, dd, J = 12.5, 0.9 Hz, H-6′), 4.41 (1H, br d, H-4′), 4.53 (1H, m, H-2), 5.33 (1H, d, J = 3.7 Hz, H-1′), 5.45 (1H, dd, J = 10.4, 7.4 Hz, H-2′), 5.48 (1H, dd, J = 7.3, 14.7 Hz, H-4), 5.53 (1H, t, J = 7.3 Hz, H-3), 5.60 (1H, s, -OCHO-), 5.64 (1H, d, J = 9.3 Hz, -NH-), 5.78 (1H, dt, J = 14.7, 6.7 Hz, H-5), 7.32–7.46, 7.54–7.60 and 7.97–8.04 (15H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3440 (NH), 3050, 2980, 2930 and 2850 (C–H), 1720, 1675 (C=O). Anal. calcd for $C_{76}H_{115}NO_{14}$: C, 72.06; H, 9.15; N, 1.11. Found: C, 72.13; H, 9.11; N, 1.29.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 51a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-2-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene **50a** (0.241 g, 0.19 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.177 g, 80%) as a colorless gum. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.24–1.31 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.38–1.47 (2H, m, -CH_2-), 1.44 (18H, s, 2×-O*t*Bu), 1.50–1.57 (4H, m, -$(CH_2)_2$-), 1.66–1.81 (2H, m, -CH_2-$CH(CO_2tBu)_2$), 1.98–2.14 (4H, m, =CH-CH_2- and -NHCOCH_2-), 2.48 (1H, br s, -OH-6′), 2.78 (1H, s, -OH-4′), 2.99 (1H, t, J = 7.5 Hz, -$CH(CO_2tBu)_2$), 3.56 (1H, dt, J = 9.3, 6.2 Hz, -OCH_2-), 3.67 (1H, dt, J = 9.3, 6.5 Hz, -OCH_2-), 3.75 (1H, dd, J = 11.1, 6.0 Hz, H-1), 3.81 (1H, dd, J = 11.1, 3.9 Hz, H-1), 3.84 (1H, dd, J = 10.3, 3.3 Hz, H-3′), 3.85–3.91 (1H, m, H-6′), 3.96–4.01 (2H, m, H-6′ and H-5′), 4.20 (1H, br d, H-4′), 4.54 (1H, m, H-2), 5.20 (1H, d, J = 3.8 Hz, H-1′), 5.31 (1H, dd, J = 10.1, 3.8 Hz, H-2′), 5.49 (1H, dd, J = 15.0, 7.3 Hz, H-4), 5.55 (1H, br t, H-3), 5.81 (1H, d, J = 10.0 Hz, -NH-), 5.82 (1H, dt overlapped by -NH-, H-5), 7.40–7.46, 7.54–7.60 and 7.98–8.01 (10H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3700–3430 (NH and OH), 3050, 2980, 2930 and 2850 (C–H), 1720, 1675 (C=O).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-2-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene 52a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-benzoyl-α-D-galactopyranosyloxy]-4-octadecene **51a** (0.175 g, 0.148 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.094 g, 57%) as a white solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, br t, 2× -CH_3), 1.24 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.56–1.63, 1.77–1.88, 1.99–2.04 and 2.20 (4H and 3×2H,

-$(CH_2)_2$-, -CH_2-, -CH_2-CH$(CO_2H)_2$ and =CH-CH_2-), 2.41 (2H, t, J = 7.4 Hz, -NHCOCH_2-), 3.57–3.50 (1H, m, -OCH_2-), 3.69–3.72 (2H, m, -OCH_2- and -$CH(CO_2H)_2$), 4.04 (1H, dd, J = 10.3, 6.9 Hz, H-1), 5.28 (1H, dd, J = 10.4, 1.9 Hz, H-3′), 4.41–4.50 (3H, m, H-6′ and H-1), 4.58 (1H, t, J = 5.9 Hz, H-5), 4.71 (1H, br s, H-4′), 5.23 (1H, m, H-2), 5.62 (1H, d, J = 3.5 Hz, H-1′), 5.92 (1H, dd, J = 15.4, 7.3 Hz, H-4), 6.07 (1H, dt, J = 15.4, 6.5 Hz, H-5), 6.13 (1H, dd, J = 10.4, 3.4 Hz, H-2′), 6.24 (1H, br t, H-3), 7.36–7.40, 7.47–7.52, 8.16–8.18 and 8.36–8.71 (10H, 4 sets of m, aromatic H), 8.85 (1H, d, J = 8.9 Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}): 3650–3100 (broad, NH and OH), 2930 and 2850 (C-H), 1720, 1650 (C=O). MS (ESI^-) 1064.7 $(M-H)^-$. MS (ESI^+) 1088.6 $(M+Na)^+$. **Sodium salt:** ^{1}H NMR (400 MHz, CD_3OD) δ 0.84 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.20–1.28 (48H, m, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.39–1.54, 1.79 and 1.93–2.07 (4H, 2H and 4H, -$(CH_2)_2$-, -CH_2-CH$(CO_2Na)_2$, =CH-CH_2- and -NHCOCH_2-), 2.96 (1H, br t, -$CH(CO_2Na)_2$), 3.43–3.48 (1H, m, -OCH_2-), 3.53 (1H, dd, J = 10.6, 6.0 Hz, H-1), 3.63 (1H, m, -OCH_2-), 3.67 and 3.71 (2H, 2 d, J = 11.4 Hz, H-6′), 3.82 (1H, dd, J = 10.5, 3.5 Hz, H-3′), 3.85–3.89 (2H, m, H-5′ and H-1), 4.12 (1H, br s, H-4′), 4.74 (1H, m, H-2), 5.03 (1H, d, J = 3.7 Hz, H-1′), 5.19 (1H, dd, J = 10.3, 3.7 Hz, H-2′), 5.40–5.49 (2H, m, H-3 and H-4), 5.77 (1H, dt, J = 14.3, 6.7 Hz, H-5), 7.34–7.42, 7.50–7.55, 7.84–7.86 and 7.91–7.93 (10H, 4 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3650-3100 (broad, NH and OH), 2920 and 2850 (C–H), 1720, 1595 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-2-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 52b

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 45b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **44b** was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.506 g, 68%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87–0.91 (6H, m, 2×-CH_3), 1.23–1.31 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.39–1.52 (4H, m, -$(CH_2)_2$-), 1.44 and 1.45 (18H, 2 s, 2×-O*t*Bu), 1.64–1.71, 1.76–1.91 and 1.96–2.03 (2H, 4H and 2H, -NHCOCH_2-, =CH-CH_2-, -CH_2-CH$(CO_2t$Bu$)_2$ and -CH_2-), 3.08 (1H, t, J = 7.5 Hz, -$CH(CO_2t$Bu$)_2$), 3.36 (1H, br s, H-5′), 3.43 (1H, dd, J = 9.6, 3.5 Hz, H-3′), 3.57 (1H, dt, J = 9.1, 6.6 Hz, -OCH_2-), 3.60–3.79 (2H, m, H-1 and -OCH_2-), 3.76 (1H, dd, J = 9.6, 7.8 Hz, H-2′), 3.79 (3H, s, -OCH_3), 4.05 (1H, dd, J = 11.6, 1.2 Hz, H-6′), 4.22–4.29 (1H, d overlapped by H-1 and H-4′, H-6′), 4.24 (1H, dd, J = 11.1, 3.2 Hz, H-1), 4.25 (1H, d, J = 3.5 Hz, H-4′), 4.32 (1H, d, J = 7.8 Hz, H-1′), 4.45 (1H, m, H-2), 4.64 and 4.78 (2H, 2 d, J = 10.4 Hz, -OCH_2Ar), 5.48 (1H, dd, J = 15.3, 7.3 Hz, H-4), 5.54 (1H, s, -OCHO-), 5.60 (1H, t, J = 7.3 Hz, H-3), 5.83 (1H, dt, J = 15.3, 6.7 Hz, H-5), 6.19 (1H, d, J = 9.1 Hz, -NH-), 6.85–6.87, 7.22–7.28, 7.32–7.45, 7.52–7.56 and 8.05–8.07 (14H, 5 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}): 3440 (NH), 3050, 2990, 2930 and 2860 (C–H), 1720, 1670 (C=O). Anal. calcd for $C_{77}H_{119}NO_{14}\cdot 0.3\ H_2O$: C, 71.79; H, 9.36; N, 1.09. Found: C, 71.84; H, 9.26; N, 1.20.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene 48b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **45b** (0.502 g, 0.39 mmol) was reacted by the procedure used to synthesize compound **48a** and afforded the title compound (0.403 g, 89%) as an amorphous beige solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.24–1.36 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.38–1.50 (2H, m, -CH_2-), 1.45 and 1.45 (18H, 2 s, 2×-O*t*Bu), 1.53–1.71 (4H, m, -$(CH_2)_2$-), 1.77–1.85, 1.96–2.05 and 2.16 (3×2H, -NHCOCH_2-, =CH-CH_2- and -CH_2-CH$(CO_2t$Bu$)_2$), 3.10 (1H, t, J = 7.4 Hz, -CH-$(CO_2t$Bu$)_2$), 3.12 (1H, br s, -OH), 3.34 (1H, dd, J = 9.6, 3.4 Hz, H-3′), 3.42 (1H, br s, H-5′), 3.54 (1H, dt, J = 9.1, 6.6 Hz, -OCH_2-), 3.71 (1H, dt, J = 9.1, 6.6 Hz, -OCH_2-), 3.81 (1H, dd, J = 11.4, 3.9 Hz, H-1), 3.89 (1H, dd, J = 9.6, 7.8 Hz, H-2′), 4.07 (1H, dd, J = 12.3, 1.3 Hz, H-6′), 4.18 (1H, dd, J = 11.4, 4.8 Hz, H-1), 4.26 (1H, d, J = 3.2 Hz, H-4′), 4.30 (1H, d, J = 12.3 Hz, H-6′), 4.34 (1H, d, J = 7.8 Hz, H-1′), 4.49 (1H, m, H-2), 5.51 (1H, dd, J = 15.3, 7.2 Hz, H-4), 5.53 (1H, s, -OCHO-), 5.62 (1H, br t, H-3), 5.87 (1H, dt, J = 15.3, 6.7 Hz, H-5), 6.42 (1H, d, J = 9.1 Hz, -NH-), 7.30–7.37, 7.41–7.45, 7.48–7.57 and 8.03–8.05 (10H, m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3550–3300 (NH and OH), 3050, 2980, 2930 and 2860 (C–H), 1720, 1670 (C=O). Anal. calcd for $C_{69}H_{111}NO_{13}$: C, 71.28; H, 9.62; N, 1.20. Found: C, 71.08; H, 9.54; N, 1.35.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-2-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 50b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **48b** (0.350 g, 0.305 mmol) was reacted by the procedure used to synthesize compound **18** and afforded the title compound (0.277 g, 72%) as a white gummy solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, br t, 2×-CH_3), 1.11–1.40 and 1.47–1.57 (52H, 2 sets of m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$- and -$(CH_2)_2$-), 1.41 and 1.42 (18H, 2 s, 2×-O*t*Bu), 1.65 (2H, m, -CH_2-CH$(CO_2t$Bu$)_2$), 1.79 (2H, br t, -NHCOCH_2-), 1.99 (2H, qa, J = 6.9 Hz, =CH-CH_2-), 2.87 (1H, t, J = 7.5 Hz, -$CH(CO_2t$Bu$)_2$), 3.45 (1H, dt, J = 9.5, 6.6 Hz, -OCH_2-), 3.49 (1H, br s, H-5′), 3.62–3.68 (1H, m overlapped by H-3′, -OCH_2-), 3.66 (1H, dd, J = 10.0, 3.2 Hz, H-3′), 3.78 (1H, dd, J = 10.4, 4.0 Hz, H-1), 4.09 (1H, dd overlapped by H-1, H-6′), 4.12 (1H, dd, J = 10.4, 4.3 Hz, H-1), 4.27 (1H, d, J = 12.0 Hz, H-6′), 4.33 (1H, d, J = 3.2 Hz, H-4′), 4.41 (1H, m, H-2), 4.61 (1H, d, J = 7.9 Hz, H-1′), 5.49 (1H, dd, J = 15.3, 7.1 Hz, H-4), 5.53 (1H, dd, J = 10.0, 8.0 Hz, H-2′), 5.57 (1H, s, -OCHO-), 5.58 (1H, t, J = 6.9 Hz, H-3), 5.81 (1H, dt, overlapped by -NH-, H-5), 5.84 (1H, d, J = 8.8 Hz, -NH-), 7.35–7.58 and 8.00–8.05 (15H, 2 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930, 2850 (C–H),

1722, 1670 (C=O). Anal. calcd for $C_{76}H_{125}NO_{14}$: C, 72.06; H, 9.15; N, 1.11. Found: C, 72.30; H, 9.12; N, 1.27.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 51b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-2-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene **50b** (0.257 g, 0.2 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.190 g, 81%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, br t, 2×-CH_3), 1.24–1.75 (55H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-, -$(CH_2)_2$-, -CH_2-CH$(CO_2t$Bu$)_2$ and -OH), 1.44 and 1.43 (18H, 2 s , 2×-O*t*Bu), 1.92 (2H, J = 7.4 Hz, -NHCOCH_2-), 2.01 (2H, dt, J = 6.9, 6.9 Hz, =CH-CH_2-), 2.93 (1H, t, J = 7.4 Hz, -CH-$(CO_2t$Bu$)_2$), 3.09 (1H, br s, -OH), 3.46 (1H, dt, J = 9.5, 6.4 Hz, -OCH_2-), 3.43–3.53 and 3.62–3.67 (2×2H, 2 sets of m, -OCH_2-, H-1 and H-5′), 3.73 (1H, dd, J = 12.2, 3.6 Hz, H-6′), 3.93 (1H, dd, J = 12.2, 6.2 Hz, H-6′), 3.98 (1H, dd, J = 9.8, 2.6 Hz, H-3′), 4.12 (1H, br d, H-4′), 4.44 (1H, m, H-2), 4.48 (1H, d, J = 7.9 Hz, H-1′), 5.42 (1H, dd, J = 9.7, 8.1 Hz, H-2′), 5.49 (1H, dd, J = 15.3, 7.9 Hz, H-4), 5.67 (1H, t, J = 7.8 Hz, H-3), 5.82 (1H, d, J = 9.4 Hz, -NH-), 5.89 (1H, dt, J = 15.3, 6.9 Hz, H-5), 7.33–7.47, 7.52–7.60 and 8.02–8.06 (10H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3700–3400 (O–H), 3050, 2980, 2930, 2850 (C–H), 1722, 1670 (C=O).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-2-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene 52b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-benzoyl-β-D-galactopyranosyloxy]-4-octadecene **51b** (0.182 g, 0.15 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.155 g, 97%) as a beige solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.20–1.29 and 1.49–1.75 (46H and 6H, 2 sets of m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$- and -$(CH_2)_2$-), 1.93 and 2.07–2.21 (2H and 4H, 2 sets of m, -NHCOCH_2-, =CH-CH_2-, -CH_2-CH$(CO_2H)_2$), 3.46 (1H, m, -OCH_2-), 3.62 (1H, t, J = 7.4 Hz, -CH$(CO_2H)_2$), 3.71 (1H, m, -OCH_2-), 3.86 (1H, dd, J = 9.9, 2.9 Hz, H-3′), 4.11 (1H, dd, J = 6.2, 6.2 Hz, H-5′), 4.30 (1H, dd, J = 10.6, 5.1 Hz, H-1), 4.37–4.42 (2H, m, H-1 and H-6′), 4.48 (1H, dd, J = 10.8, 6.2 Hz, H-6′), 4.68 (1H, d, J = 2.7 Hz, H-4′), 5.11 (1H, m, H-2), 5.13 (1H, d, J = 7.9 Hz, H-1′), 5.80 (1H, dd, J = 15.5, 7.2 Hz, H-4), 5.92 (1H, dt, J = 15.5, 6.6 Hz, H-5), 6.13 (1H, br t, H-3), 6.26 (1H, dd, J = 9.8, 8.1 Hz, H-2′), 7.36–7.39, 7.45–7.54, 8.19–8.21 and 8.32–8.36 (11H, 4 sets of m, aromatic H and -NH-). IR (nujol) ν_{max} (cm^{-1}) 3700–2400 (O–H, N–H), 2930, 2850 (broad, C-H), 1720, 1650 (C=O). MS (ESI^-) 1064.4 $(M-H)^-$. MS (ESI^+) 1088.7 $(M+Na)^+$. **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 0.83 (6H, br t, 2×-CH_3), 1.14–1.46 (52H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$- and -$(CH_2)_2$-), 1.67 and 1.80–1.95 (2H and 4H, 2 sets of m, -NHCOCH_2-, -CH_2-CH$(CO_2Na)_2$ and =CH–CH_2-), 2.93 (1H, t, J = 7.1 Hz, -CH$(CO_2Na)_2$), 3.38 (1H, m, -OCH_2-), 3.54–3.72 (6H, m, -OCH_2-, H-6′, H-1, H-5′ and H-3′), 3.93 (1H, dd, J = 9.9, 6.3 Hz, H-6′), 4.06 (1H, br s, H-4′), 4.33 (1H, m, H-2), 4.56 (1H, d, J = 8.0 Hz, H-1′), 5.29 (1H, br dd, H-2′), 5.38 (1H, dd, J = 15.0, 7.7 Hz, H-4), 5.44 (1H, br t, H-3), 5.66 (1H, dt, J = 15.0, 6.9 Hz, H-5), 7.37–7.43, 7.51–7.53 and 7.91–7.98 (10H, 3 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3700–2400 (O–H, N–H), 2930, 2850 (broad, C–H), 1720, 1650, 1600 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-4-octadecene 54a

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-α-D-galactopyranosyloxy]-4-octadecene 53a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-4-octadecene **48a** (0.260 g, 0.22 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.173 g, 74%) as a gummy white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2× -CH_3), 1.26–1.37 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.41–1.51 (2H, m, -CH_2-), 1.47 (18H, s, 2×-O*t*Bu), 1.53–1.73 (4H, m, -$(CH_2)_2$-), 1.82–1.88 (2H, m, -CH_2-CH$(CO_2t$Bu$)_2$), 2.05 (2H, dt, J = 6.9, 6.9 Hz, =CH-CH_2-), 2.20 (2H, m, -NHCOCH_2-), 2.68 (1H, br s, -OH), 3.15 (1H, t, J = 7.4 Hz, -CH$(CO_2t$Bu$)_2$), 3.45 (1H, dd, J = 9.7, 3.2 Hz, H-3′), 3.62–3.71 (2H, m, -OCH_2-), 3.77 (1H, dd, J = 11.1, 5.7 Hz, H-1), 3.82–3.99 (5H, m, H-1, H-2′, H-5′ and H-6′), 4.12 (1H, d, J = 3.0 Hz, H-4′), 4.56 (1H, m, H-2), 4.90 (1H, d, J = 3.9 Hz, H-1′), 5.53 (1H, dd, J = 15.3, 7.4 Hz, H-4), 5.63 (1H, br t, H-3), 5.90 (1H, dt, J = 15.3, 6.9 Hz, H-5), 5.96 (1H, d, J = 9.3 Hz, -NH-), 7.45–7.49, 7.58–7.62 and 8.03–8.05 (5H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3700–3400 (NH and OH), 3050, 2980, 2930 and 2860 (C–H), 1720, 1675 (C=O).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-4-octadecene 54a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-α-D-galactopyranosyloxy]-4-octadecene **53a** (0.165 g, 0.154 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.124 g, 80%) as a white solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, t, J = 6.7 Hz, 2× -CH_3), 1.24–1.36 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.64–1.75 (4H, m, -$(CH_2)_2$-), 1.84 (2H, m, -CH_2-), 2.04 (2H, dt, J = 6.8, 6.8 Hz, = CH-CH_2-), 2.28 (2H, m, -CH_2-CH$(CO_2H)_2$), 2.47 (2H, t, J = 7.4 Hz, -NHCOCH_2-), 3.51–3.53 and 3.72–3.74 (2× 1H, 2 sets of m, -OCH_2-), 3.83 (1H, t, J = 7.4 Hz, -CH$(CO_2H)_2$), 3.96 (1H, dd, J = 10.0, 3.0 Hz, H-3-), 4.17 (1H, dd, J = 10.8, 6.6 Hz, H-6′), 4.35–4.53 (4H, m, H-6′, H-1 and H-5′), 4.60 (1H, br d, H-4′), 4.68 (1H, dd, J = 10.0, 3.8 Hz, H-2′), 5.22 (1H, m, H-2), 5.36 (1H, d, J = 3.8 Hz, H-1′), 5.97 (1H, dd, J = 15.5, 7.1 Hz, H-4), 6.13 (1H, dt, J = 15.5, 6.8 Hz, H-5), 6.36 (1H, br t, H-3), 7.39–7.43, 7.50–7.53 and 8.24–8.26 (5H, 3 sets of m, aromatic H), 8.91 (1H, d, J = 8.7 Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}) 3650–3100 (NH and OH), 2930, 2850 (C-H), 1730, 1640 (C=O). MS (ESI^-) 960.6 $(M-H)^-$. MS (ESI^+) 962.7 (MH^+), 984.7 $(M+Na)^+$. **Sodium**

salt: IR (nujol) ν_{max} (cm^{-1}) 3650-3100 (broad, NH and OH), 2920 and 2850 (broad, C-H), 1710, 1640 and 1585 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-hydroxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-4-octadecene 57a. A solution of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-4-octadecene **54a** (0.291 g, 0.3 mmol) in dry dichloromethane (20 mL) was treated with a solution of sodium methoxide in methanol (0.0276 g of sodium in 1.5 mL of methanol) at 5 °C. The mixture was stirred at 23 °C for 1 h, then cooled down to 5 °C and treated with Dowex 50W8 resin H^+ until the pH reached ~6.0–6.5. The resin was filtered and washed with dichloromethane/methanol (1:1, 3×5 mL). The combined filtrate and washings were concentrated and co-evaporated with toluene (4×5 mL). The residue was purified by silica gel chromatography (30 g, 0–10% methanol/ethyl acetate and traces of pyridine then 11:1:88 to 50:20:30 methanol/water/ethyl acetate) to give the title compound (0.152 g, 56%) as a white solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.85 (6H, m, 2×-CH_3), 1.25–1.38, 1.68, 1.85 and 2.08 (46H, 4H, 2H and 2H, 4 sets of m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-, -$(CH_2)_2$- and -C*H*$_2$CH$(CO_2H)_2$), 2.28 (2H, dt, *J* = 7.2, 7.2 Hz, =CH-C*H*$_2$-), 2.48 (2H, m, -NHCOC*H*$_2$-), 3.50 and 3.72 (2×1H, 2 sets of m, -OCH_2-), 3.82 (1H, t, *J* = 7.4 Hz, -CH$(CO_2H)_2$), 3.93 (1H, dd, *J* = 9.9, 3.0 Hz, H-3′), 4.35 (1H, dd, *J* = 10.5, 5.2 Hz, H-1 or H-6′), 4.41–4.51 (4H, m, H-1, H-5′ and H-6′), 4.61 (1H, br d, *J* = 2.6 Hz, H-4′), 4.66 (1H, dd, *J* = 9.9, 3.9 Hz, H-2′), 4.83–4.89 (2H, m, H-2 and H-3), 5.41 (1H, d, *J* = 3.9 Hz, H-1′), 6.00 and 6.03 (2×1H, 2 d, *J* = 15.4 Hz, H-4 and H-5), 8.59 (1H, d, *J* = 8.3 Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}) 3650–3100 (NH and OH), 2920, 2850 (C–H), 1715, 1645 (C=O). **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 0.85 (6H, t, *J* = 6.8 Hz, 2×-CH_3), 1.24–1.42, 1.54–1.64, 1.78–1.84 (48H, 4H and 2H, 3 sets of m, -$(CH_2)_{11}$- and -$(CH_2)_{13}$-, -$(CH_2)_2$- and -C*H*$_2$CH-$(CO_2Na)_2$), 1.96 (2H, dt *J* = 6.8, 6.8 Hz, =CH-C*H*$_2$-), 2.15 (2H, t, *J* = 7.5 Hz, -NHCOC*H*$_2$-), 3.06 (1H, t, *J* = 7.4 Hz, -C*H*$(CO_2Na)_2$), 3.46–3.53 and 3.64–3.73 (2H and 5H, 2 sets of m, -OCH_2-, H-1, H-3′, H-5′ and H-6′), 3.77 (1H, dd, *J* = 10.8, 3.8 Hz, H-1 or H-6′), 3.82 (1H, dd, *J* = 10.0, 3.8 Hz, H-2′), 3.87 (1H, dt, *J* = 8.5, 3.4 Hz, H-2), 4.04 (1H, br d, *J* = 2.0 Hz, H-4′), 4.08 (1H, t, *J* = 8.2 Hz, H-3), 4.81 (1H, d, *J* = 3.9 Hz, H-1′), 5.39 (1H, dd, *J* = 15.3, 7.5 Hz, H-4), 5.67 (1H, dt, *J* = 15.3, 6.8 Hz, H-5). IR (nujol) ν_{max} (cm^{-1}) 3700–3050 (NH and OH), 2920, 2850 (C–H), 1645 (C=O). MS (ESI^-) 856.6 ($M-H)^-$. MS (ESI^+) 858.7 (MH^+), 880.6 $(M+Na)^+$.

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-β-D-galactopyranosyloxy]-4-octadecene 54b

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-β-D-galactopyranosyloxy]-4-octadecene 53b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-4-octadecene **48b** (0.397 g, 0.34 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.308 g, 84%) as a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, *J* = 6.7 Hz, 2×-CH_3), 1.25–1.35 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.40–1.49 (2H, m, -CH_2-), 1.47 (18H, s, 2×-O*t*Bu), 1.53–1.71 (4H, 2 sets of m, -$(CH_2)_2$-), 1.84, 2.04 and 2.19 (3×2H, 3 sets of m, -NHCOC*H*$_2$-, =CH–C*H*$_2$- and -C*H*$_2$-CH$(CO_2t$Bu$)_2$), 2.77 and 2.90 (2H, 2 br s, 2× -OH), 3.13–3.17 (1H, br s, -OH), 3.15 (1H, t, *J* = 7.4 Hz, -CH$(CO_2t$Bu$)_2$), 3.24 (1H, dd, *J* = 9.4 and 3.2 Hz, H-3′), 3.45 (1H, br dd, H-5′), 3.59 (1H, dt, *J* = 9.2, 6.5 Hz, -OCH_2-), 3.68–3.77 (3H, m, -OCH_2-, H-6′ and H-2′), 3.82 (1H, dd, *J* = 11.2, 4.3 Hz, H-1), 3.93 (1H, dd, *J* = 12.0, 6.0 Hz, H-6′), 4.02–4.06 (2H, m, H-1 and H-4′), 4.30 (1H, d, *J* = 7.7 Hz, H-1′), 4.56 (1H, m, H-2), 5.51 (1H, dd, *J* = 15.3, 7.5 Hz, H-4), 5.65 (1H, br t, H-3), 5.90 (1H, dt, *J* = 15.3, 6.7 Hz, H-5), 6.13 (1H, d, *J* = 9.4 Hz, -NH-), 7.44–7.48, 7.53–7.61 and 8.03–8.05 (5H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3700–3300 (NH and OH), 3050, 2980, 2930 and 2850 (C–H), 1720, 1670 (C=O). Anal. calcd for $C_{62}H_{107}NO_{13}\cdot 0.5H_2O$: C, 68.73; H, 10.05; N, 1.29. Found: C, 68.79; H, 9.92; N, 1.45.

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-carboxypentyl)-β-D-galactopyranosyloxy]-4-octadecene 54b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-β-D-galactopyranosyloxy]-4-octadecene **53b** (0.290 g, 0.27 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.142 g, 55%) as a white solid. ^{1}H NMR (400 MHz, pyridine-d_5) δ 0.86 (6H, t, *J* = 6.6 Hz, 2×-CH_3), 1.24–1.37 (46H, m, -$(CH_2)_{13}$- and -$(CH_2)_{10}$-), 1.70–1.86, 1.98 and 2.30 (6H and 2×2H, -$(CH_2)_2$-, -CH_2-, =CH-C*H*$_2$- and -C*H*$_2$CH$(CO_2H)_2$), 2.44 (2H, t, *J* = 7.4 Hz, -NHCOC*H*$_2$-), 3.65 (1H, dd, *J* = 9.3, 3.0 Hz, H-3′), 3.63–3.71 (1H, m, -OCH_2-), 3.83 (1H, t, *J* = 7.4 Hz, -CH$(CO_2H)_2$), 3.81–3.87 (1H, m, -OCH_2-), 4.02 (1H, dd, *J* = 6.0, 6.0 Hz, H-5′), 4.15 (1H, dd, *J* = 10.9, 4.4 Hz, H-1), 4.39 (1H, dd, *J* = 10.9, 6.0 Hz, H-6′), 4.45 (1H, dd, *J* = 10.9, 6.0 Hz, H-6′), 4.51 (1H, br dd, H-2′), 4.57 (1H, dd, *J* = 10.9, 5.1 Hz, H-1), 4.59 (1H, br d, *J* = 2.8 Hz, H-4′), 4.89 (1H, d, *J* = 7.7 Hz, H-1′), 5.11 (1H, m, H-2), 5.88 (1H, dd, *J* = 15.4, 7.4 Hz, H-4), 6.02 (1H, dt, *J* = 15.4, 6.5 Hz, H-5), 6.20 (1H, br t, H-3), 7.35–8.22 (5H, m, aromatic H), 8.70 (1H, d, *J* = 10.9 Hz, -NH-). IR (nujol) ν_{max} (cm^{-1}) 3700–3000 (NH and OH), 2920 and 2850 (broad, C-H), 1715, 1630 (C=O). MS (ESI^-) 960.6 $(M-H)^-$. MS (ESI^+) 984.7 $(M+Na)^+$. **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 0.89 (6H, t, *J* = 6.8 Hz, 2×-CH_3), 1.27–1.43 (48H, m, -$(CH_2)_{13}$- and -$(CH_2)_{11}$-), 1.58–1.66 (4H, m, -$(CH_2)_2$-), 1.84, 2.05, and 2.18–2.24 (3×2H, -NHCOC*H*$_2$-, =CH-C*H*$_2$- and -C*H*$_2$-CH$(CO_2Na)_2$), 3.09 (1H, t, *J* = 7.1 Hz, -CH$(CO_2Na)_2$), 3.20 (1H, dd, *J* = 9.6, 3.0 Hz, H-3′), 3.42–3.75 (7H, m, H-2′, H-5′, H-6′, -OCH_2- and H-1), 4.01 (1H, br d, H-4′), 4.13 (1H, dd, *J* = 10.4, 5.0 Hz, H-1), 4.22 (1H, d, *J* = 7.7 Hz, H-1′), 4.42 (1H, m, H-2), 5.51 (1H, dd, *J* = 15.0, 7.8 Hz, H-4), 5.58 (1H, br t, H-3), 5.89 (1H, dt, *J* = 15.0, 6.8 Hz, H-5), 7.45–7.48, 7.57–7.61 and 8.00–8.02 (5H, 3 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3700–3000 (NH), 2920 and 2850 (broad, C–H), 1715, 1585 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-carboxyethyl)benzyl]-α-D-galactopyranosyloxy}-4-octadecene 56a

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy}-4-octadecene 46a and (2*S*,3*R*,4*E*)-3-benzoyloxy-2-azido-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy}-4-octadecene 46b. Ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-1-thio-β-D-galactopyranoside **27** (0.500 g, 0.666 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-benzoyloxy-4-octadecen-1-ol **28** (0.258 g, 0.6 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** except that acetonitrile was used as solvent. This afforded the α-anomer (0.114 g, 15%) and the β-anomer (0.111 g, 15%) of the title compound as oils. **α-Anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.7 Hz, -CH_3), 1.26–1.36 (22H, m, -$(CH_2)_{11}$-), 1.42 (18H, s, 2×-O*t*Bu), 2.07 (2H, dt, J = 6.9, 6.9 Hz, =CH–CH_2-), 3.13 (2H, d, J = 7.8 Hz, -CH_2-CH(CO_2tBu)$_2$), 3.45 (1H, t, J = 7.8 Hz, -CH(CO_2tBu)$_2$), 3.59 (1H, dd, J = 10.9, 7.4 Hz, H-1), 3.65 (1H, br s, H-5′), 3.73 (1H, dd, J = 10.9, 4.6 Hz, H-1), 3.79 (3H, s, -OCH_3), 3.93–3.98 (2H, m, H-2 and H-3′), 4.02 (1H, d, J = 12.2 Hz, H-6′), 4.06 (1H, dd, J = 10.2, 3.4 Hz, H-2′), 4.15 (1H, d, J = 3.0 Hz, H-4′), 4.20 (1H, d, J = 12.2 Hz, H-6′), 4.60 and 4.76 (2×1H, 2 d, J = 11.6 Hz, -OCH_2Ar), 4.69 and 4.79 (2×1H, 2 d, J = 12.1 Hz, -OCH_2Ar), 4.89 (1H, d, J = 3.3 Hz, H-1′), 5.48 (1H, s, -OCHO-), 5.58 (1H, dd, J = 14.7, 8.0 Hz, H-4), 5.63 (1H, dd, J = 8.0, 4.1 Hz, H-3), 5.91 (1H, dt, J = 14.7, 6.9 Hz, H-5), 6.82–6.84, 7.17–7.19, 7.27–7.39, 7.45–7.61 and 8.07–8.09 (18H, 5 sets of m, aromatic H). **β-Anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.8 Hz, -CH_3), 1.24–1.36 (22H, m, -$(CH_2)_{11}$-), 1.42 (2×9H, 2 s, 2×-O*t*Bu), 2.04 (2H, dt, J = 6.9, 6.9 Hz, =CH-CH_2-), 3.13 (2H, d, J = 7.8 Hz, -CH_2-CH(CO_2tBu)$_2$), 3.30 (1H, br s, H-5′), 3.45 (1H, t, J = 7.8 Hz, -CH(CO_2tBu)$_2$), 3.52 (1H, dd, J = 9.6, 3.5 Hz, H-3′), 3.61 (1H, dd, J = 9.7, 5.1 Hz, H-1), 3.79 (3H, s, -OCH_3), 3.85 (1H, dd, J = 9.6, 7.7 Hz, H-2′), 3.98–4.07 (4H, m, H-1, H-2, H-4′ and H-6′), 4.28 (1H, d, J = 12.0 Hz, H-6′), 4.38 (1H, d, J = 7.7 Hz, H-1′), 4.68–4.87 (4H, m, 2×-OCH_2Ar), 5.49 (1H, s, -OCHO-), 5.58 (1H, dd, J = 15.3, 8.0 Hz, H-4), 5.70 (1H, dd, J = 8.0, 3.6 Hz, H-3), 5.90 (1H, dt, J = 15.3, 6.9 Hz, H-5), 6.85–6.88, 7.16–7.18, 7.28–7.48, 7.55–7.60 and 8.07–8.09 (18H, 5 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy}-4-octadecene 47a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)-benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy}-4-octadecene **46a** (0.114 g, 0.102 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.099 g, 74%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.24–1.26 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.42 (18H, s, 2×-O*t*Bu), 1.48–1.61 (2H, m, -CH_2-), 1.98–2.14 (4H, m, -NHCOCH_2- and =CH-CH_2-), 3.13 (2H, d, J = 7.8 Hz, -CH_2-CH(CO_2tBu)$_2$), 3.44 (1H, t, J = 7.8 Hz, -CH(CO_2tBu)$_2$), 3.65 (1H, br s, H-5′), 3.78 (3H, s, -OCH_3), 3.78–3.79 (2H, m, H-1), 3.92 (1H, dd, J = 10.1, 3.4 Hz, H-3′), 4.00 (1H, br d, H-6′), 4.05 (1H, dd, J = 10.1, 3.5 Hz, H-2′), 4.18–4.21 (2H, m, H-4′ and H-6′), 4.48 (1H, m, H-2), 4.63–4.75 (4H, m, 2×-OCH_2Ar), 3.91 (1H, d, J = 3.5 Hz, H-1′), 5.47 (1H, s, -OCHO-), 5.48 (1H, dd, J = 15.3, 7.5 Hz, H-4), 5.60 (1H, br t, J = 7.3 Hz, H-3), 5.79 (1H, dt, J = 15.3, 6.9 Hz, H-5), 5.99 (1H, d, J = 9.1 Hz, -NH-), 6.79–6.82, 7.17–7.21, 7.27–7.52, 7.57–7.60 and 8.04–8.06 (18H, 5 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-4,6-*O*-benzylidene-α-D-galactopyranosyloxy}-4-octadecene 49a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy}-4-octadecene **47a** (0.135 g, 0.103 mmol) was reacted by the procedure used to synthesize compound **48a** and afforded the title compound (0.112 g, 91%) as a sticky solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2× -CH_3), 1.26–1.42 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.42 (18H, s, 2×-O*t*Bu), 1.60 (2H, m, -CH_2-), 2.05 (2H, m, =CH-CH_2-), 2.18 (2H, m, -NHCOCH_2-), 2.36 (1H, br s, -OH), 3.12 (2H, d, J = 7.9 Hz, -CH_2–CH(CO_2tBu)$_2$), 3.42 (1H, t, J = 7.9 Hz, -CH(CO_2tBu)$_2$), 3.69 (1H, s, H-5′), 3.71–3.76, 4.18–4.24 and 3.92 (2H, 2H, 1H, 2 sets of m and 1 dd, J = 10.9, 3.7 Hz, H-2′, H-3′, H-1 and H-4′), 4.02 (1H, br d, J = 12.1 Hz, H-6′), 4.23 (1H, br d, H-6′), 4.55 (1H, m, H-2), 4.70 and 4.72 (2×1H, 2 d, J = 12.3 Hz, -OCH_2Ar), 4.99 (1H, d, J = 3.7 Hz, H-1′), 5.45 (1H, s, -OCHO-), 5.52 (1H, dd, J = 15.3, 7.3 Hz, H-4), 5.62 (1H, br t, H-3), 5.85 (1H, d, J = 8.4 Hz, -NH-), 5.84–5.91 (1H, dt overlapped by -NH-, H-5), 7.16–7.18, 7.31–7.40, 7.44–7.52, 7.58–7.61 and 8.03–8.05 (14H, 5 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-α-D-galactopyranosyloxy}-4-octadecene 55a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-4,6-*O*-benzylidene-α-D-galactopyranosyloxy}-4-octadecene **49a** (0.112 g, 0.09 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.071 g, 68%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.26–1.37 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.43 (18H, s, 2×-O*t*Bu), 1.60 (2H, m, -CH_2-), 2.05 (2H, dt, J = 7.0, 7.0 Hz, =CH-CH_2-), 2.20 (2H, m, -NHCOCH_2-), 2.38 and 2.50 (2H and 1H, 2 br s, 2× -OH), 3.14 (2H, d, J = 7.8 Hz, -CH_2–CH(CO_2tBu)$_2$), 3.45 (1H, t, J = 7.8 Hz, -CH(CO_2tBu)$_2$), 3.60 (1H, dd, J = 9.7, 3.2 Hz, H-3′), 3.73 (1H, dd, J = 11.1, 5.8 Hz, H-1), 3.80–3.93 (4H, m, H-1, H-6′ and H-5′), 3.96 (1H, dd, J = 9.6, 3.8 Hz, H-2′), 4.03 (1H, br d, J = 2.9 Hz, H-4′), 4.56 (1H, m, H-2), 4.66 and 4.79 (2×1H, 2d, J = 11.6 Hz, -OCH_2Ar), 4.89 (1H, d, J = 3.9 Hz, H-1′), 5.53 (1H, dd, J = 15.3, 7.3 Hz, H-4), 5.63 (1H, br t, H-3), 5.89 (1H, dt, J = 15.3, 7.0 Hz, H-5), 5.94 (1H, d, J = 9.2 Hz, -NH-), 7.21–7.23, 7.29–7.31,

7.45–7.49, 7.58–7.62 and 8.03–8.05 (9H, 5 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-α-D-galactopyranosyloxy}-4-octadecene 56a. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl] - α - D - galactopyranosyloxy}-4-octadecene **55a** (0.071 g, 0.063 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.059 g, 89%) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) δ 0.89 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.26 (48H, m, -$(CH_2)_{11}$- and -$(CH_2)_{13}$-), 2.06 (2H, m, =CH-CH_2-), 2.20 (2H, m, -NHCOCH_2-), 3.14 (2H, d, J = 7.7 Hz, -CH_2-CH$(CO_2H)_2$), 3.58–3.69 (6H, 2 sets of m, H-1, -6′, -5′, H-3′ and -CH-$(CO_2H)_2$), 3.84 (1H, dd, J = 10.9, 4.3 Hz, H-1), 3.92 (1H, dd, J = 10, 3.8 Hz, H-2′), 4.03 (1H, d, J = 2.8 Hz, H-4′), 4.43–4.45 (1H, m, H-2), 4.60 and 4.69 (2×1H, 2 d, -OCH_2Ar), 4.78 (1H, d, J = 3.9 Hz, H-1′), 5.53 (1H, dd, J = 15.1, 7.7 Hz, H-4), 5.61 (1H, br t, H-3), 5.88 (1H, dt, J = 15.1, 6.9 Hz, H-5), 7.21–7.23, 7.34–7.36, 7.45–7.49, 7.58–7.61 and 8.01–8.03 (9H, 4 sets of m, aromatic H). **Sodium salt:** ^{1}H NMR (400 MHz, CD_3OD) δ 0.89 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.26–1.40 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.60 (2H, m, -CH_2-), 2.06 (2H, dt, J = 6.8, 6.8 Hz, =CH-CH_2-), 2.21 (2H, t, J = 7.3 Hz, -NHCOCH_2-), 3.23–3.30 (2H, m, -CH_2-CH$(CO_2Na)_2$), 3.60–3.77 (6H, m, H-1, H-6′, H-3′, H-5′ and -CH-$(CO_2Na)_2$), 3.83 (1H, dd, J = 10.9, 4.1 Hz, H-1), 3.91 (1H, dd, J = 10.0, 3.9 Hz, H-2′), 4.01 (1H, d, J = 2.7 Hz, H-4′), 4.44 (1H, m, H-2), 4.60 and 4.67 (2×1H, 2 d, J = 11.5 Hz, -OCH_2Ar), 4.77–4.79 (1H, d, J = 3.9 Hz, H-1′), 5.53 (1H, dd, J = 15.1, 7.9 Hz, H-4), 5.62 (1H, br t, H-3), 5.89 (1H, dt, J = 15.1, 6.8 Hz, H-5), 7.19–7.23, 7.30–7.33, 7.45–7.49, 7.58–7.62 and 8.02–8.04 (9H, 5 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3700–3100 (O–H and N–H), 2920, 2860 (C–H), 1710, 1630 (C=O).

Synthesis of (2*S*,3*R*,4*E*)-3-benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-carboxyethyl)benzyl]-β-D-galactopyranosyloxy}-4-octadecene 56b

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy}-4-octadecene 47b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-azido-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)-benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy}-4-octadecene **46b** (0.111 g, 0.10 mmol) was reacted by the procedure used to synthesize compound **30a** and afforded the title compound (0.064 g, 65%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.6 Hz, 2×-CH_3), 1.23–1.35 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.41 (18H, s, 2×-O*t*Bu), 1.41–1.51 (2H, m, -CH_2-), 1.86 (2H, m, -NHCOCH_2-), 2.00 (2H, m, J = 6.9 Hz, =CH-CH_2-), 3.13 (2H, d, J = 7.8 Hz, -CH_2CH$(CO_2t$Bu$)_2$), 3.29 (1H, br s, H-5′), 3.44 (1H, t, J = 7.8 Hz, -CH$(CO_2t$Bu$)_2$), 3.53 (1H, dd, J = 9.5, 3.5 Hz, H-3′), 3.70 (1H, dd, J = 11.3, 4.0 Hz, H-1), 3.80 (3H, s, -OCH_3), 3.84 (1H, br t, H-2′), 4.00 (1H, d, J = 11.6 Hz, H-6′), 4.08 (1H, d, J = 3.4 Hz, H-4′), 4.22 (1H, dd, J = 11.3, 3.4 Hz, H-1), 4.24 (1H, d, J = 11.6 Hz, H-6′), 4.31 (1H, d, J = 7.8 Hz, H-1′), 4.46 (1H, m, H-2), 4.68 and 4.80 (2×1H, 2 d, 2×-OCH_2Ar), 4.71 and 4.74 (2×1H, 2 d, J = 12.2 Hz, -OCH_2Ar), 5.48 (1H, s, -OCHO-), 5.48 (1H, dd, J = 15.3, 7.4 Hz, H-4), 5.61 (1H, br t, H-3), 5.83 (1H, dt, J = 15.3, 6.7 Hz, H-5), 6.16 (1H, d, J = 9.1 Hz, -NH-), 6.84–6.86, 7.16–7.18, 7.25–7.31, 7.33–7.44, 7.52–7.56 and 8.05–8.07 (18H, 6 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-4,6-*O*-benzylidene-β-D-galactopyranosyloxy}-4-octadecene 49b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy}-4-octadecene **47b** (0.124 g, 0.094 mmol) was reacted by the procedure used to synthesize compound **48a** and afforded the title compound (0.080 g, 85%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2× -CH_3), 1.25–1.42 (46H, m, -$(CH_2)_{11}$- and -$(CH_2)_{12}$-), 1.42 (18H, s, 2×-O*t*Bu), 1.58–1.61 (2H, m, -CH_2-), 2.03 (2H, dt, J = 6.9, 6.9 Hz, = CH-CH_2-), 2.16 (2H, m, -NHCOCH_2-), 3.13 (2H, d, J = 7.8 Hz, -CH_2–CH$(CO_2t$Bu$)_2$), 3.35 (1H, s, H-5′), 3.42–3.46 (2H, m, H-3′ and -CH-$(CO_2t$Bu$)_2$), 3.82 (1H, dd, J = 11.4, 3.8 Hz, H-1), 3.96 (1H, dd, J = 9.4, 7.8 Hz, H-2′), 4.01 (1H, br d, H-6′), 4.08 (1H, d, J = 3.3 Hz, H-4′), 4.14 (1H, dd, J = 11.4, 5.5 Hz, H-1), 4.26 (1H, d, J = 12.3 Hz, H-6′), 4.31 (1H, d, J = 7.7 Hz, H-1′), 4.50 (1H, m, H-2), 4.73 (2H, s, -OCH_2Ar), 5.45 (1H, s, -OCHO-), 4.51 (1H, dd, J = 15.3, 7.2 Hz, H-4), 5.61 (1H, br t, H-3), 5.87 (1H, dt, J = 15.3, 6.9 Hz, H-5), 6.29 (1H, d, J = 9.1 Hz, -NH-), 7.17–7.19, 7.27–7.38, 7.41–7.45, 7.50–7.57 and 8.03–8.05 (14H, 5 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-β-D-galactopyranosyloxy}-4-octadecene 55b. (2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-4,6-*O*-benzylidene-β-D-galactopyranosyloxy}-4-octadecene **49b** (0.097 g, 0.08 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.068 g, 76%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, J = 6.7 Hz, 2×-CH_3), 1.25–1.42 (48H, m, -$(CH_2)_{11}$- and -$(CH_2)_{13}$-), 1.42 (18H, s, 2×-O*t*Bu), 2.02–2.07 (2H, m, =CH-CH_2-), 2.10–2.25 (2H, m, -NHCOCH_2-), 2.79, 2.85 and 3.06 (3×1H, 3 s, 3×-OH), 3.13 (2H, d, J = 7.9 Hz, -CH_2-CH$(CO_2t$Bu$)_2$), 3.37 (1H, dd, J = 9.4, 3.3 Hz, H-3′), 3.40 (1H, br dd, H-5′), 3.45 (1H, t, J = 7.8 Hz, -CH$(CO_2t$Bu$)_2$), 3.73 (1H, br d, H-6′), 3.79 (1H, dd, J = 9.4, 7.9 Hz, H-2′), 3.83 (1H, dd, J = 11.1, 4.3 Hz, H-1), 3.90 (1H, dd, J = 11.8, 5.6 Hz, H-6′), 3.96 (1H, br d, H-4′), 4.00 (1H, dd, J = 11.1, 5.1 Hz, H-1), 4.28 (1H, d, J = 7.7 Hz, H-1′), 4.57 (1H, m, H-2), 4.72 (2H, s, -OCH_2Ar), 5.51 (1H, dd, J = 15.3, 7.4 Hz, H-4), 5.65 (1H, br t, H-3), 5.91 (1H, dt, J = 15.3, 6.9 Hz, H-5), 6.02 (1H, d, J = 9.3 Hz, -NH-), 7.20–7.22, 7.27–7.30, 7.44–7.48, 7.57–7.61 and 8.03–8.05 (9H, 5 sets of m, aromatic H).

(2*S*,3*R*,4*E*)-3-Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-β-D-galactopyranosyloxy}-4-octadecene 56b. (2*S*,3*R*,4*E*)-3-

Benzoyloxy-2-hexadecanoylamino-1-{3-*O*-[4-(2,2-di-*tert*-butyloxycarbonylethyl)benzyl]-β-D-galactopyranosyloxy}-4-octadecene **55b** (0.068 g, 0.061 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.067 g, quant.) as a white foam. **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 0.89 (6H, t, J = 6.8 Hz, 2×-CH_3), 1.26–1.39 (46H, m, -$(CH_2)_{11}$- and -$CH_2)_{12}$-), 1.59 (2H, m, -CH_2-), 2.06 (2H, dt, J = 6.8, 6.8 Hz, =CH-CH_2-), 2.19 (2H, m, -NH-COCH_2-), 3.14 (2H, d, J = 7.7 Hz, -CH_2CH$(CO_2H)_2$), 3.34 (1H, dd, J = 9.7, 3.2 Hz, H-3′), 3.40 (1H, br dd, H-5′), 3.58–3.71 (5H, m, -CH$(CO_2H)_2$, H-1, H-6′ and H-2′), 3.98 (1H, d, J = 2.9 Hz, H-4′), 4.10 (1H, dd, J = 10.4, 5.3 Hz, H-6′), 4.22 (1H, d, J = 7.7 Hz, H-1′), 4.44 (1H, m, H-2), 4.61 and 4.72 (2×1H, 2 d, J = 11.7 Hz, -OCH_2Ar), 5.51 (1H, dd, J = 14.9, 7.8 Hz, H-4), 5.57 (1H, br t, H-3), 5.89 (1H, dt, J = 14.9, 6.8 Hz, H-5), 7.20–7.22, 7.35–7.37, 7.43–7.48, 7.57–7.61 and 7.99–8.02 (9H, 5 sets of m, aromatic H). IR (nujol) ν_{max} (cm^{-1}) 3700–3100 (O–H and N–H), 2920, 2860 (C–H), 1715, 1630 (C=O).

Synthesis of methyl 9-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-nonanoate 60a

Methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate 59a and methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-4,6-*O*-benzylidene-3-*O*-benzoyl-β-D-galactopyranosyloxy]-nonanoate 59b. Ethyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside **20** (0.800 g, 1.21 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (0.500 g, 2.42 mmol) and methyl 9-hydroxynonanoate **58** (0.228 g, 1.21 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** except that dioxane was used as solvent. This afforded the α-anomer (0.503 g, 53%) and the β-anomer (0.528 g, 56%) of the title material as oils. **α-Anomer**: $[\alpha]_D^{22}$ +112° (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33–1.43 and 1.62–1.68 (8H and 4H, -$(CH_2)_6$-), 1.40 and 1.41 (2×9H, 2s, 2×-O*t*Bu), 2.04 (2H, m, -CH_2CH$(CO_2t$Bu$)_2$), 2.32 (2H, t, J = 7.5 Hz, -CH_2CO_2Me), 3.38 (1H, t, J = 7.5 Hz, -CH$(CO_2t$Bu$)_2$), 3.57 (1H, dt, J = 9.7, 6.6 Hz, -OCH_2-), 3.66–3.68 (2H, m, -OCH_2-), 3.68 (3H, s, -OMe), 3.75 (1H, dt, J = 9.7, 7.0 Hz, -OCH_2-), 3.84 (1H, s, H-5), 4.08–4.12 (2H, m, H-6′ and H-2′), 4.30 (1H, dd, J = 12.4, 1.0 Hz, H-6′), 3.62 (1H, d, J = 3.3 Hz, H-4′), 5.13 (1H, d, J = 3.4 Hz, H-1′), 5.46 (1H, dd, J = 10.5, 3.6 Hz, H-3′), 3.52 (1H, s, -OCHO-), 7.32–7.34, 7.43–7.49, 7.53–7.59 and 8.10–8.12 (10H, 4 sets of m, aromatic H). Anal. calcd for $C_{43}H_{60}O_{13}\cdot 0.1CH_2Cl_2$: C, 65.24; H, 7.65. Found: C, 65.10; H, 7.48. **β-Anomer**: $[\alpha]_D^{22}$ +54° (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22–1.38 and 1.64 (8H and 4H, 2 sets of m, -$(CH_2)_6$-), 1.38 (18H, s, 2× -O*t*Bu), 2.00 (2H, m, -CH_2CH$(CO_2t$Bu$)_2$), 2.31 (2H, t, J = 7.5 Hz, -CH_2CO_2Me), 3.31 (1H, t, J = 7.4 Hz, -CH$(CO_2t$Bu$)_2$), 3.44–3.56 (1H, m, -OCH_2-), 3.54 (1H, s, H-5′), 3.62–3.68 (1H, m, -OCH_2-), 3.68 (3H, s, -OCH_3), 3.80 (1H, dd, J = 10.1, 7.7 Hz, H-2′), 3.90 (1H, dt, J = 10.1, 6.0 Hz, -OCH_2-), 3.97 (1H, dt, J = 9.1, 6.9 Hz, -OCH_2-), 4.08 (1H, d, J = 12.1 Hz, H-6′), 4.35 (1H, d, J = 12.1 Hz, H-6′), 4.44 (1H, d, J = 7.7 Hz, H-1′), 4.49 (1H, d, J = 3.6 Hz, H-4′), 5.08 (1H, dd, J = 10.1, 3.6 Hz, H-3′), 5.50 (1H, s, -OCHO-), 7.32–7.36, 7.40–7.49, 7.53–7.59 and 8.08–8.14 (10H, 3 sets of m, aromatic H). IR (film) ν_{max} (cm^{-1}) 2980, 2930, 2860 (C–H), 1730 (C=O). Anal. calcd for $C_{43}H_{60}O_{13}\cdot 0.1CH_2Cl_2$: C, 65.24; H, 7.65. Found: C, 65.01; H, 7.49.

Methyl 9-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-α-D-galactopyranosyloxy]-nonanoate 60a. Anisole (0.30 mL) was added to neat methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate **59a** (0.412 g, 0.52 mmol) at 0 °C. 90% Aqueous trifluoroacetic acid (15 mL) was then added and the mixture was stirred at 0 °C for 5 min, then toluene (15 mL) was added. The solvents were evaporated and the co-evaporation was repeated twice. The same procedure was repeated again and the residue was purified by silica gel chromatography (3×6 cm, 2.5–30% methanol/chloroform +5% water) and afforded the title compound (0.175 g, 58%) as a solid. MS (ESI^-) 583.2 $(M-H)^-$. MS (ESI^+) 585.4 $(MH)^+$, 607.2 $(M+Na)^+$. HRMS (ESI^-) calcd for $C_{28}H_{39}O_{13}$: 583.23905. Found: 583.2399 δ = −1.4 ppm. **Diacid**: ^{1}H NMR (400 MHz, pyridine-d_5) δ 1.17–1.21, 1.28–1.34, 1.53–1.68 (6H, 2H and 4H, -$(CH_2)_6$-), 2.28 (2H, t, J = 7.4 Hz, -CH_2CO_2Me), 2.69 (2H, dt, J = 6.5, 6.5 Hz, -CH_2CH$(CO_2H)_2$), 3.58 (3H, s, -OCH_3), 3.65 (1H, dt, J = 9.3, 6.6 Hz, -OCH_2-), 3.94 (1H, dt, J = 9.3, 6.8 Hz, -OCH_2-), 4.18 (2H, t, J = 6.1 Hz, -OCH_2-), 4.29 (1H, t, J = 7.3 Hz, -CH$(CO_2H)_2$), 4.41 (1H, dd, J = 10.6, 6.2 Hz, H-6′), 4.46 (1H, dd, J = 10.6, 6.2 Hz, H-6′), 4.52 (1H, br dd, J = 6.0, 6.0 Hz, H-5′), 4.80 (1H, dd, J = 10.4, 3.5 Hz, H-2′), 5.08 (1H, d, J = 2.8 Hz, H-4′), 5.58 (1H, d, J = 3.5 Hz, H-1′), 6.03 (1H, dd, J = 10.4, 2.8 Hz, H-3′), 7.29–7.40 and 8.26–8.28 (5H, 2 sets of m, aromatic H). **Sodium salt:** ^{1}H NMR (400 MHz, CD_3OD) δ 1.29 and 1.55–1.61 (8H and 4H, -$(CH_2)_6$-), 2.03 (2H, m, -CH_2CH$(CO_2Na)_2$), 2.26 (2H, br t, -CH_2CO_2Me), 3.04 (1H, t, J = 6.5 Hz, -CH$(CO_2Na)_2$), 3.46 (1H, br dt, -OCH_2-), 3.53–3.64 (4H, m, H-6′ and -OCH_2-), 3.58 (3H, s, -OCH_3), 3.60 (1H, br dt, -OCH_2-), 3.85 (1H, dd, J = 5.6, 5.6 Hz, H-5′), 3.99 (1H, br d, J = 10.5 Hz, H-2′), 4.13 (1H, br s, H-4′), 5.03 (1H, br s, H-1′), 5.17 (1H, br d, J = 10.5 Hz, H-3′), 7.40–7.44, 7.51–7.54 and 8.01–8.03 (5H, 3 sets of m, aromatic H). IR (KBr) ν_{max} (cm^{-1}) 3700–3000 (O–H), 3030 and 2960 (C–H), 1720 (C=O) and 1580.

Synthesis of methyl 9-[2-*O*-(3,3-di-carboxypropyl)-3-*O*-benzoyl-β-D-galactopyranosyloxy]-nonanoate 60b.

Methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate **59b** (0.52 g, 0.66 mol) was reacted by the general procedure used to synthesize compound **33a** and afforded the title compound (0.191 g, 50%) as a white foam. **Diacid**: ^{1}H NMR (400 MHz, pyridine-d_5) δ 1.28–1.32, 1.52–1.57 and 1.66–1.73 (8H, 2H and 2H, 3 sets of m, -$(CH_2)_6$-), 2.28 (2H, t, J = 7.5 Hz, -CH_2CO_2Me), 2.74 (2H, m, -CH_2CH$(CO_2H)_2$), 3.61 (3H, s, -OCH_3), 3.69 (1H, dt, J = 9.2, 6.9 Hz, -OCH_2-), 4.06 (1H, dt, J = 9.2, 6.9 Hz, -OCH_2-), 4.10 (1H, dd, J = 6.1, 6.1 Hz, H-5′), 4.22–4.30 and 4.38–4.51 (4H and 2H, 2 sets of m, H-6′, -OCH_2-, H-2′ and -CH$(CO_2H)_2$), 4.83 (1H, d, J = 7.6 Hz, H-1′), 4.96 (1H, d, J = 3.0 Hz, H-4′), 5.60 (1H, dd, J = 10.1, 3.1 Hz, H-3′), 7.29–7.39 and 8.25–8.31

(5H, 2 sets of m, aromatic H). Anal. calcd for $C_{28}H_{40}O_{13}\cdot 0.25\ H_2O$: C, 56.48; H, 6.86. Found: C, 56.42; H, 6.74. MS (ESI^-) 583.3 $(M-H)^-$. **Sodium salt**: ^1H NMR (400 MHz, CD_3OD) δ 1.26–1.33 and 1.52–1.59 (8H and 4H, -$(CH_2)_6$-), 1.91–2.06 (2H, m, -C*H*$_2$-CH$(CO_2Na)_2$), 2.25 (2H, t, $J=7.4$ Hz, -CH_2CO_2Me), 2.99 (1H, t, $J=7.4$ Hz, -CH$(CO_2Na)_2$), 3.50–3.67 and 3.80–3.86 (6H and 2H, 2×-OCH_2-, H-2′, H-4′, H-5′ and H-6′), 3.58 (3H, s, -OCH_3), 4.08 (1H, d, $J=3.2$ Hz, H-4′), 4.35 (1H, d, $J=7.7$ Hz, H-1′), 4.85 (1H, dd, $J=10.1$, 3.3 Hz, H-3′), 7.40–7.44, 7.50–7.54 and 8.01–8.03 (5H, 3 sets of m, aromatic H). IR (KBr) ν_{max} (cm^{-1}) 3700–3000 (O-H), 2930, 2850 (C–H), 1720 (C=O) and 1580.

Synthesis of methyl 9-[2-*O*-(3,3-di-carboxypropyl)-α-D-galactopyranosyloxy]-nonanoate 62a

Methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-α-D-galactopyranosyloxy]-nonanoate 61a and methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-β-D-galactopyranosyloxy]-nonanoate 61b. Ethyl 3,4-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-1-thio-β-D-galactopyranoside **12** (0.900 g, 1.45 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (0.600 g, 2.90 mmol), methyl 9-hydroxynonanoate **58** (0.273 g, 1.45 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** and afforded a mixture of α- and β-anomers of the title material (0.900 g, 83%) as a yellow oil. This mixture was dissolved in dry tetrahydrofuran (10 mL) and was treated with acetic acid (0.4 mL) and tetrabutylammonium fluoride (1 M in tetrahydrofuran, 5 mL, 5 mmol) at 0 °C. The mixture was stirred 45 min at 0 °C and 1 h at 23 °C. Tetrabutylammonium fluoride (2.5 mL) was added again and the mixture was stirred for two additional h at 23 °C and stored at −20 °C overnight. The mixture was diluted with toluene and co-evaporated (2×). The residue was dissolved in ethyl acetate (100 mL) and washed with aqueous saturated sodium bicarbonate (2×50 mL), water (50 mL) and brine, dried over anhydrous sodium sulfate, filtered and concentrated. The residue was purified by silica gel chromatography (3.5×14 cm, 30–50% ethyl acetate/hexane) and afforded the α-anomer (0.306 g, 40%) and the β-anomer (0.280 g, 37%) of the title compound as clear oils. **α-Anomer**: $[\alpha]_D^{22}$ +60° (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.31–1.35 and 1.61–1.62 (8H and 4H, 2 sets of m, -$(CH_2)_6$-), 1.35 and 1.52 (2×3H, 2 s, -$C(CH_3)_2$-), 1.46 (18H, s, 2×-O*t*Bu), 2.04–2.15 (2H, m, -C*H*$_2$-CH$(CO_2tBu)_2$), 2.31 (2H, t, $J=7.5$ Hz, -C*H*$_2CO_2Me$), 3.41 (1H, t, $J=7.4$ Hz, -CH$(CO_2tBu)_2$), 3.42 (1H, dd, $J=7.7$, 3.4 Hz, H-2′), 3.47 (1H, dt, $J=9.7$, 6.6 Hz, -OCH_2-), 3.58–3.70 (3H, m, H-5′ and -OCH_2-), 3.68 (3H, s, -OCH_3), 3.74 (1H, dt, $J=9.9$, 6.0 Hz, -OCH_2-), 3.96 (1H, dd, $J=11.7$, 6.1 Hz, H-6′), 4.04–4.07 (1H, br d, H-6′), 4.23 (1H, dd, $J=5.6$, 2.6 Hz, H-4′), 4.28 (1H, dd, $J=7.6$, 5.7 Hz, H-3′), 4.91 (1H, d, $J=3.4$ Hz, H-1′). IR (film) ν_{max} (cm^{-1}) 3650–3200 (O-H), 2980, 2930, 2860 (C-H), 1740, 1725 (C=O). **β-Anomer**: $[\alpha]_D^{22}$ +10° (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.27–1.31 and 1.61–1.62 (8H and 4H, 2 sets of m, -$(CH_2)_6$-), 1.33 and 1.51 (2×3H, 2 s, -$C(CH_3)_2$-), 1.46 and 1.47 (2×9H, 2 s, 2×-O*t*Bu), 2.05–2.11 (2H, m, -C*H*$_2$CH$(CO_2tBu)_2$), 2.31 (2H, t, $J=7.5$ Hz, -CH_2CO_2Me), 3.23 (1H, br dd, H-2′), 3.43 (1H, t, $J=7.3$ Hz, -CH$(CO_2tBu)_2$), 3.49 (1H, dt, $J=9.3$, 6.9 Hz, -OCH_2-), 3.67 (3H, s, -OCH_3), 3.71 (1H, dt, $J=9.9$, 6.1 Hz, -OCH_2-), 3.78–3.85 (3H, m, H-5′, H-6′ and -OCH_2-), 3.87 (1H, dt, $J=9.3$, 6.9 Hz, -OCH_2-), 3.94–4.00 (1H, m, H-6′), 4.09 (1H, dd, $J=6.4$, 5.9 Hz, H-3′), 4.13 (1H, dd, $J=5.8$, 1.2 Hz, H-4′), 4.23 (1H, d, $J=7.9$ Hz, H-1′). IR (film) ν_{max} (cm^{-1}) 3700–3200 (O–H), 2980, 2935, 2860 (C–H), 1740, 1725 (C=O).

Methyl 9-[2-*O*-(3,3-dicarboxypropyl)-α-D-galactopyranosyloxy]-nonanoate 62a. Methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-β-D-galactopyranosyloxy]-nonanoate **61a** (0.291 g, 0.46 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title compound (0.095 g, 43%) as a yellow oil. **Diacid:** ^1H NMR (400 MHz, pyridine-d_5) δ 1.16, 1.28–1.34, 1.52–1.61, 1.63–1.71 (6H, 2H, 2H and 2H, 4 sets of m, -$(CH_2)_6$-), 2.27 (2H, t, $J=7.5$ Hz, -CH_2CO_2Me), 2.72 (2H, dt, $J=6.4$, 6.4 Hz, -$CH_2CH(CO_2H)_2$), 3.60 (3H, s, -OCH_3), 3.60 (1H, dt, $J=9.5$, 6.5 Hz, -OCH_2-), 3.94 (1H, dt, $J=9.3$, 6.7 Hz, -OCH_2-), 4.08–4.18, 4.31–4.45 (2H and 5H, 2 sets of m, -OCH_2-, H-6′, H-5′, H-2′ and -$CH(CO_2H)_2$), 4.58 (1H, dd, $J=9.7$, 3.2 Hz, H-3′), 4.61 (1H, d, $J=3.2$ Hz, H-4′), 5.46 (1H, d, $J=3.5$ Hz, H-1′). **Sodium salt:** ^1H NMR (400 MHz, CD_3OD) δ 1.27 and 1.55 (8H and 4H, 2 sets of m, -$(CH_2)_6$-), 2.03–2.08 (2H, m, -C*H*$_2$-CH$(CO_2Na)_2$), 2.26 (2H, t, $J=7.4$ Hz, -C*H*$_2$-CO_2Me), 3.20 (1H, t, $J=7.4$ Hz, -CH$(CO_2Na)_2$), 3.39 (1H, dt, $J=9.5$, 6.4 Hz, -OCH_2-), 3.48 (1H, dt, $J=9.2$, 7.3 Hz, -OCH_2-), 3.54 (1H, dd, $J=10.0$, 3.5 Hz, H-2′), 3.59 (3H, s, -OCH_3), 3.62–3.73 (5H, m, -OCH_2-, H-6′ and H-5′), 3.75 (1H, dd, $J=10.0$, 3.2 Hz, H-3′), 3.83 (1H, br d, $J=2.6$ Hz, H-4′), 4.92 (1H, d, H-1′). IR (KBr) ν_{max} (cm^{-1}) 3800–3000 (O–H), 2940 (C–H), 1740 (C=O) and 1580.

Synthesis of methyl 9-[2-*O*-(3,3-di-carboxypropyl)-β-D-galactopyranosyloxy]-nonanoate 62b. A solution of methyl 9-[2-*O*-(3,3-di-*tert*-butyloxycarbonylpropyl)-3,4-*O*-isopropylidene-β-D-galactopyranosyloxy]-nonanoate **61b** (0.207 g, 0.33 mmol) was reacted by the procedure used to synthesize compound **33a** and gave the title material (0.100 g, 63%) as a white solid. **Diacid**: ^1H NMR (400 MHz, pyridine-d_5) δ 1.15, 1.29–1.32, 1.51–1.57 and 1.64–1.71 (6H and 3×2H, 4 sets of m, -$(CH_2)_6$-), 2.28 (2H, t, $J=7.5$ Hz, -C*H*$_2CO_2Me$), 2.78 (2H, m, -C*H*$_2$CH$(CO_2H)_2$), 3.61 (3H, s, -OCH_3), 3.66, 4.03–4.11 and 4.50–4.55 (1H, 3H and 1H, 3 sets of m, -OCH_2-, H-5′, H-4′ and H-3′), 3.97 (1H, t, $J=5.9$ Hz, -CH$(CO_2H)_2$), 4.21 (1H, dt, $J=9.6$, 6.0 Hz, -OCH_2-), 4.39 (1H, br t, H-2′), 4.42 (2H, d, $J=6.1$ Hz, H-6′), 4.53 (1H, dt, $J=9.9$, 6.0 Hz, -OCH_2-), 4.71 (1H, d, $J=6.7$ Hz, H-1′). **Sodium salt**: ^1H NMR (400 MHz, CD_3OD) δ 1.27 and 1.53–1.55 (8H and 4H, 2 sets of m, -$(CH_2)_6$-), 1.98–2.10 (2H, m, -C*H*$_2$CH$(CO_2Na)_2$), 2.26 (2H, t, $J=7.4$ Hz, -C*H*$_2CO_2Me$), 3.18–3.26, 3.44–3.54, 3.82–3.86 and 3.95–3.98 (2H, 3H, 1H and 1H, 4 sets of m, 2×-OCH_2-, H-2′, H-3′ and H-5′), 3.39 (1H, t, $J=5.9$ Hz, -CH$(CO_2Na)_2$), 3.59 (3H, s, -OCH_3), 3.67 (2H, d, $J=6.1$ Hz, H-6′), 3.78 (1H, d, $J=2.7$ Hz, H-4′),

4.18 (1H, d, $J=7.7$ Hz, H-1′). IR (KBr) ν_{max} (cm^{-1}) 3800–3000 (O–H), 2935, 2860 (C–H), 1740 (C=O), 1600.

Synthesis of methyl 9-[3-*O*-(5,5-di-carboxypentyl)-β-D-galactopyranosyloxy]-nonanoate 66b

Methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate 63a and methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-nonanoate 63b. A solution of ethyl 2-*O*-*p*-methoxybenzyl-4,6-di-*O*-benzylidene-3-(5,5-di-*tert*-butyloxycarbonylpentyl)-1-thio-β-D-galactopyranoside **26** (0.98 g, 1.4 mmol), methyl 9-hydroxy-nonanoate **58** (0.265 g, 1.4 mmol) and 2,6-di-*tert*-butyl-4-methyl-pyridine (0.580 g, 2.8 mmol) were reacted by the procedure used to synthesize compounds **29a** and **b** to give the α-anomer (0.469 g, 40%) and the β-anomer (0.598 g, 51%) of the title material as oils. **α-Anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27–1.50 and 1.56–1.77 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.45 (18H, 2 s, 2×-O*t*Bu), 1.82 (2H, m, -C*H*$_2$-CH(CO_2*t*Bu)$_2$), 2.31 (2H, t, $J=7.5$ Hz, -C*H*$_2CO_2$Me), 3.10 (1H, t, $J=7.5$ Hz, -C*H*(CO_2*t*Bu)$_2$), 3.44 (1H, dt, $J=9.9$, 6.7 Hz, -OCH_2-), 3.58–3.72 (3H, m, 3×-OCH_2-), 3.65 (1H, s, H-5′), 3.68 (3H, s, -OCH_3), 3.81 (3H, s, -OCH_3), 3.81–3.84 (1H, dd overlapped by -OCH_3, H-3′), 3.93 (1H, dd, $J=10.1$, 3.5 Hz, H-2′), 4.06 (1H, dd, $J=12.3$, 1.3 Hz, H-6′), 4.22 (1H, dd, $J=12.3$, 1.1 Hz, H-6′), 4.32 (1H, d, $J=3.0$ Hz, H-4′), 4.55 and 4.77 (2×1H, 2 d, $J=11.7$ Hz, -OCH_2Ar), 4.81 (1H, d, $J=3.5$ Hz, H-1′), 5.54 (1H, s, -OCHO-), 6.84–6.88, 7.27–7.38 and 7.50–7.52 (9H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930 and 2860 (C–H), 1722 (C=O). **β-anomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27–1.47 and 1.57–1.68 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.45 (18H, s, 2×-O*t*Bu), 1.79–1.85 (2H, m, -C*H*$_2$CH(CO_2*t*Bu)$_2$), 2.30 (2H, t, $J=7.5$ Hz, -C*H*$_2CO_2$Me), 3.09 (1H, t, $J=7.5$ Hz, -C*H*(CO_2*t*Bu)$_2$), 3.37 (1H, s, H-5′), 3.41 (1H, dd, $J=9.7$, 3.6 Hz, H-3′), 3.51 (1H, dt, $J=9.4$, 7.0 Hz, -OCH_2-), 3.60 (1H, dt, $J=9.4$, 6.7 Hz, -OCH_2-), 3.65–3.74 (1H, m overlapped by -OCH_3, -OCH_2-), 3.67 (3H, s, -OCH_3), 3.72 (1H, dd, $J=9.7$, 7.8 Hz, H-2′), 3.81 (3H, s, -OCH_3), 3.98 (1H, dt, $J=9.3$, 6.5 Hz, -OCH_2-), 4.07 (1H, dd, $J=12.2$, 1.4 Hz, H-6′), 4.23 (1H, d, $J=3.4$ Hz, H-4′), 4.33 (1H, dd, $J=12.2$, 0.8 Hz, H-6′), 4.37 (1H, d, $J=7.8$ Hz, H-1′), 4.67 and 4.82 (2×1H, 2 d, $J=10.3$ Hz, -OCH_2Ar), 3.55 (1H, s, -OCHO-), 6.87–6.89, 7.27–7.38 and 7.53–7.55 (9H, 3 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930 and 2860 (C–H), 1722 (C=O).

Methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-nonanoate 64b. A solution of methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-nonanoate **63b** (0.586 g, 0.707 mmol) was reacted by the procedure used to synthesize compound **48a** and afforded the title compound (0.381 g, 76%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25–1.52 and 1.60–1.71 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.45 (2×9H, 2 s, 2×-O*t*Bu), 1.82 (2H, m, -C*H*$_2$CH(CO_2*t*Bu)$_2$), 1.93 (1H, br s, -OH), 2.30 (2H, t, $J=7.5$ Hz, -C*H*$_2CO_2$Me), 3.09 (1H, t, $J=7.5$ Hz, -C*H*(CO_2*t*Bu)$_2$), 3.38 (1H, dd, $J=9.7$, 3.4 Hz, H-3′), 3.42 (1H, s, H-5′), 3.54 (2H, m, -OCH_2-), 3.67 (3H, s, -OCH_3), 3.71 (1H, dt, $J=9.1$, 6.7 Hz, -OCH_2-), 3.90 (1H, dd, $J=9.7$, 7.8 Hz, H-2′), 3.94 (1H, dt, $J=9.3$, 7.0 Hz, -OCH_2-), 4.09 (1H, dd, $J=12.2$, 1.3 Hz, H-6′), 4.27 (1H, d, $J=3.4$ Hz, H-4′), 4.32 (1H, d, $J=7.8$ Hz, H-1′), 4.35 (1H, d overlapped by H-1′, H-6′, 5.55 (1H, s, -OCHO-), 7.30–7.37 and 7.50–7.53 (5H, 2 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3050, 2980, 2930 and 2870 (C–H), 1725 (C=O).

Methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-β-D-galactopyranosyloxy]-nonanoate 65b. A solution of methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-β-D-galactopyranosyloxy]-nonanoate **64b** (0.285 g, 0.402 mmol) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.089 g, 36%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24–1.56 and 1.61–1.76 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.47 (18H, s, 2×-O*t*Bu), 1.85 (2H, m, -C*H*$_2$CH(CO_2*t*Bu)$_2$), 2.31 (2H, t, $J=7.5$ Hz, -C*H*$_2CO_2$Me), 3.14 (1H, t, $J=7.4$ Hz, -CH(CO_2*t*Bu)$_2$), 3.30 (1H, dd, $J=9.4$, 3.4 Hz, H-3′), 3.52–3.57 and 3.61–3.72 (5H, 2 sets of m, H-2′, H-5′ and 3×-OCH_2-), 3.68 (3H, s, -OCH_3), 3.85 (1H, dd, $J=11.7$, 4.6 Hz, H-6′), 3.92 (1H, dt, $J=9.4$, 6.8 Hz, -OCH_2-), 4.01 (1H, dd, $J=11.7$, 6.7 Hz, H-6′), 4.05 (1H, br d, $J=3.0$ Hz, H-4′), 4.27 (1H, d, $J=7.8$ Hz, H-1′).

Methyl 9-[3-*O*-(5,5-di-carboxypentyl)-β-D-galactopyranosyloxy]-nonanoate 66b. A solution of methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-β-D-galactopyranosyloxy]-nonanoate **65b** (0.126 *g*, 0.203 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title material (0.101 g, 98%) as a white fluffy solid. **Diacid**: ^{1}H NMR (400 MHz, pyridine-d_5) δ 1.10–1.26 and 1.51–1.74 (18H, 2 sets of m, -$(CH_2)_6$-, -$(CH_2)_2$- and -C*H*$_2$CH(CO_2H)$_2$), 2.27 (2H, t, $J=7.4$ Hz, -C*H*$_2CO_2$Me), 3.57–3.66, 3.68–3.88, 4.01–4.11 and 4.44–4.48 (13H, 4 sets of m, -OCH_3, H-2′, H-3′, H-5′, H-6′, 2×-OCH_2- and -CH(CO_2H)$_2$), 4.58 (1H, br s, H-4′), 4.76 (1H, d, $J=7.6$ Hz, H-1′). IR (nujol) ν_{max} (cm^{-1}) 3700–2200 (O–H), 2920 and 2850 (C–H), 1720 (C=O). **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 1.32–1.46 and 1.59–1.66 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.90–1.96 (2H, m, -C*H*$_2$-CH(CO_2Na)$_2$), 2.30 (2H, t, $J=7.4$ Hz, -C*H*$_2CO_2$Me), 3.06 (1H, t, $J=6.2$ Hz, -CH(CO_2Na)$_2$), 3.19 (1H, dd, $J=9.6$, 3.2 Hz, H-3′), 3.43–3.74 (7H, m, H-2′, H-5′, H-6′ and 3× -OCH_2-), 3.64 (3H, s, -OCH_3), 3.87 (1H, dt, $J=9.4$, 6.8 Hz, -OCH_2-), 4.01 (1H, d, $J=2.6$ Hz, H-4′), 4.21 (1H, d, $J=7.8$ Hz, H-1′). IR (nujol) ν_{max} (cm^{-1}) 3650–3100 (O-H), 2910 (C–H), 1740 (C=O).

Synthesis of methyl 9-[3-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-nonanoate 66a

Methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate 64a. A solution of methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-2-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate **63a** (0.460 g, 0.55 mmol) in dichloromethane (30 mL) and water

(3 mL) was reacted by the procedure used to synthesize compound **48a** and afforded the title compound (0.357 g, 92%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27–1.52 and 1.64–1.71 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.45 and 1.46 (2×9H, 2 s, 2×-O*t*Bu), 1.80–1.86 (2H, m, -CH_2CH(CO_2tBu)$_2$), 2.32 (2H, t, J = 7.5 Hz, -CH_2CO_2Me), 3.11 (1H, t, J = 7.5 Hz, -CH-(CO_2tBu)$_2$), 3.50–3.57 and 3.64–3.75 (6H, 2 sets of m, 4×-OCH_2-, H-3′ and H-5′), 3.68 (3H, s, -OCH_3), 4.10 (1H, d overlapped by H-2′, H-6′), 4.12 (1H, dd, J = 9.9, 3.7 Hz, H-2′), 4.28 (1H, d, J = 12.4 Hz, H-6′), 4.34 (1H, d, J = 3.1 Hz, H-4′), 5.05 (1H, d, J = 3.7 Hz, H-1′), 5.56 (1H, s, -OCHO-), 7.31–7.37 and 7.51–7.53 (5H, 2 sets of m, aromatic H). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3060, 2940 and 2860 (C-H), 1722 (C=O).

Methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-α-D-galactopyranosyloxy]-nonanoate 65a. A solution of methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-4,6-*O*-benzylidene-α-D-galactopyranosyloxy]-nonanoate **64a** (0.274 g, 0.387 mmol) in dichloromethane (15 mL) was reacted by the procedure used to synthesize compound **40a** and afforded the title compound (0.170 g, 71%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27–1.32, 1.40–1.51 and 1.61–1.75 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.46 (18H, s, 2×-O*t*Bu), 1.81–1.87 (2H, m, -CH_2CH(CO_2tBu)$_2$), 2.31 (2H, t, J = 7.5 Hz, -CH_2–CO_2Me), 3.14 (1H, t, J = 7.4 Hz, -CH(CO_2tBu)$_2$), 3.45–3.51, 3.61–3.75 and 3.80–3.85 (2H, 2H and 1H, 3×-OCH_2-, H-6′ and H-3′), 3.68 (3H, s, -OCH_3), 3.72 (1H, dt, J = 9.6, 6.8 Hz, -OCH_2-), 3.82 (1H, s, H-5′), 3.90 (1H, dd, J = 9.6, 3.7 Hz, H-2′), 3.97 (1H, dd, J = 12.9, 7.0 Hz, H-6′), 4.13 (1H, d, J = 3.0 Hz, H-4′), 4.96 (1H, d, J = 3.9 Hz, H-1′). IR (CH_2Cl_2) ν_{max} (cm^{-1}) 3570 (O–H), 3050, 2980, 2930 and 2860 (C–H), 1720 (C=O).

Methyl 9-[3-*O*-(5,5-di-carboxypentyl)-α-D-galactopyranosyloxy]-nonanoate 66a. A solution of methyl 9-[3-*O*-(5,5-di-*tert*-butyloxycarbonylpentyl)-α-D-galactopyranosyloxy]-nonanoate **65a** (0.186 g, 0.299 mmol) was reacted by the procedure used to synthesize compound **33a** and afforded the title material (0.128 g, 98%) as a white fluffy solid. **Diacid:** ^{1}H NMR (400 MHz, pyridine-d_5) δ 1.17–1.37, 1.54–1.71 (18H, 2 sets of m, -$(CH_2)_6$-, -CH_2CH(CO_2H)$_2$ and -$(CH_2)_2$-), 2.29 (2H, t, J = 7.5 Hz, -CH_2CO_2Me), 3.52–3.68, 3.82–3.85 and 4.38–4.49 (6H, 3 sets of m, H-6′, H-5′, -OCH_2-, -CH(CO_2H)$_2$), 3.55 (1H, dt, J = 9.6, 6.6 Hz, -OCH_2-), 3.61 (3H, s, -OCH_3), 3.96 (1H, dt, J = 9.6, 6.9 Hz, -OCH_2-), 4.03 (1H, dd, J = 10.0, 3.1 Hz, H-3′), 4.68 (1H, d, J = 2.1 Hz, H-4′), 4.70 (1H, dd, J = 10.1, 3.9 Hz, H-2′), 5.31 (1H, d, J = 3.8 Hz, H-1′). IR (nujol) ν_{max} (cm^{-1}) 3500–2500 (O–H), 2920 and 2850 (C–H), 1710 (C=O). MS (ESI$^-$) 507.2 (M−H)$^-$. MS (ESI$^+$) 531.2 (M+Na)$^+$, 553.3 (M+2Na)$^+$. HRMS (ESI$^+$): calcd for $C_{23}H_{40}NaO_{12}$: 531.2417. Found: 531.2434 δ = −3.2 ppm. **Sodium salt**: ^{1}H NMR (400 MHz, CD_3OD) δ 1.28–1.53 and 1.58–1.66 (16H, 2 sets of m, -$(CH_2)_6$- and -$(CH_2)_2$-), 1.85–1.91 (2H, m, -CH_2CH(CO_2Na)$_2$), 2.30 (2H, t, J = 7.4 Hz, -CH_2CO_2Me), 3.08 (1H, t, J = 6.9 Hz, -CH(CO_2Na)$_2$), 3.43 (1H, dt, J = 9.7, 6.6 Hz, -OCH_2-), 3.46 (1H, dd, J = 10.1, 3.2 Hz, H-3′), 3.49–3.54 and 3.64–3.78 (5H, 2 sets of m, H-6′ and -OCH_2-), 3.64 (3H, s, -OCH_3), 3.70 (1H, s, H-5′), 3.82 (1H, dd, J = 10.1, 3.9 Hz, H-2′), 4.08 (1H, br d, J = 2.7 Hz, H-4′), 4.77 (1H, d, J = 3.9 Hz, H-1′). IR (nujol) ν_{max} (cm^{-1}) 3650–3100 (O–H), 2920, 2850 (C–H), 1735 (C=O).

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