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Note

Synthesis of neutral glycosphingolipids from *Zygomycetes*

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Abstract—Novel neutral glycosphingolipids (NGSLs) containing Gal-α1→6Gal, previously found in the *Zygomycetes* species *Mucor hiemalis*, were synthesized. The structures of these compounds are different from those of other fungal GSLs, and they are expected to be involved in host–parasite interactions. A key step in their synthesis is direct 1,2-cis α-selective galactosylation of 4,6-diol tri- and tetrasaccharide acceptors with a galactosyl donor in the presence of *N*-iodosuccinimide (NIS)/trifluoromethanesulfonic acid (TfOH). The fully protected glycosides were deprotected to give the two target glycosphingolipids.

Keywords: α-Galactosylation; 1,2-*cis*-Glycoside; Di-*tert*-butylsilylene group; *Zygomycetes* species; *Mucor hiemalis*

In our continuing systematic studies on the role and biological functions of glycosphingolipids, we have synthesized glycolipids found in various lower animal species.[1–5] Recently, Aoki et al. reported the discovery of one of the novel class of neutral glycosphingolipids (NGSLs), D-Gal-(α1→6)-D-Gal-(α1→6)-D-Gal-(α1→6)-D-Gal-(β1→6)-D-Gal-β1-Cer, and their precursor tri- and tetrasaccharides, in *Mucor hiemalis*, a typical *Zygomycetes* species (Fig. 1).[6] The structures of these materials are different from those of other fungal NGSLs, and their biosynthetic pathway does not exist in human beings. NGSLs can be considered as a selective target for zygomycosis toxicity, which may lead to the development of new antifungal agents featuring both superior growth inhibition of Zygomycetes and destruction of the pathogenetic factor. In our previous paper, we reported the synthesis of trisaccharide glycosphingolipids (**1**).[7] The key reaction in that synthesis was 1,2-cis α-selective galactosylation using a 4,6-*O*-di-*tert*-butylsilylene (DTBS) group, which was reported by Ando and Kiso.[8] Highly α-selective galactosylation was carried out due to the DTBS group, and the yield was further improved due to the influence of a 2-O-benzylated donor (a 2-O-benzoylated donor was previously used). In this work, we report the synthesis of tetra- and pentasaccharide glycolipids (**2**, **3**).

CDS	Galβ1-6Galβ1-Cer	
CTS	Galα1-6Galβ1-6Galβ1-Cer	**1**
CTeS	Galα1-6Galα1-6Galβ1-6Galβ1-Cer	**2**
CPS	Galα1-6Galα1-6Galα1-6Galβ1-6Galβ1-Cer	**3**

Figure 1.

It is thought that almost complete regioselective glycosylation can be achieved for a galactoside acceptor with two unprotected hydroxyl groups by making effective use of the difference in their reactivities due to their primary and secondary nature; additionally, 2,3-O-benzylated protecting groups could be transformed into the corresponding 2,3-O-benzoylated protecting groups in order to decrease the reactivity of the 4-OH group. Thus, for the synthesis of the target compounds, NGSLs **2** and **3**, core oligosaccharides **6** and **18** were selected as glycosyl acceptors, because compounds **6** and **18** each contains two free hydroxyl groups at C-4 and C-6 of the nonreducing end of the galactose residue for α-galactosylation. This greatly simplifies the preparation

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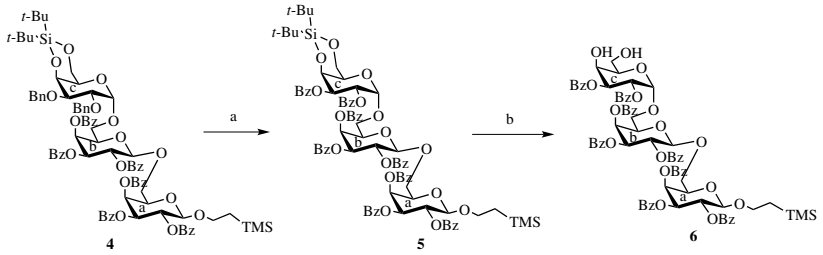


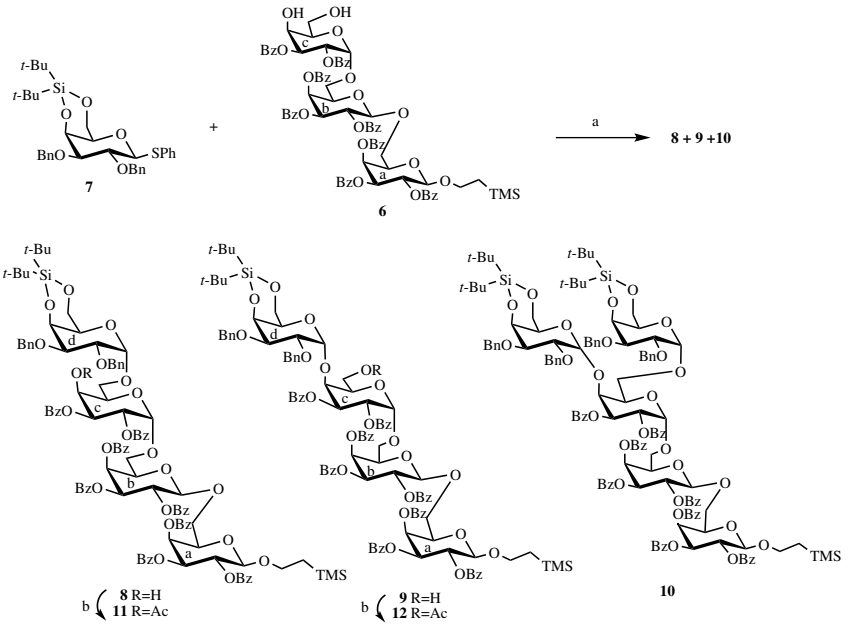
Scheme 1. Reagents and conditions: (a) (i) Pd–C, H_2, MeOH/THF, (ii) BzCl, Pyr., 86% (two steps); (b) TBAF, AcOH/THF, 95%.

of galactoside acceptors for 6-O-glycosylation without the repetition of protection and deprotection. Removal of the benzyl groups from **4**[7] by catalytic hydrogenolysis over 10% Pd–C in THF/MeOH (1:2) and subsequent benzoylation gave **5**. Selective removal of the DTBS group using tetrabutylammonium fluoride (TBAF) gave the corresponding 4,6-diol trisaccharide acceptor **6** (Scheme 1). Several examples of the conditions used for glycosylation of **6** with **7**[7] are given in Table 1. The glycosylation reactions were carried out under an Ar atmosphere in CH_2Cl_2 using 1.0–1.5 equiv of *N*-iodosuccinimide (NIS) and 0.05–0.30 equiv of trifluoromethanesulfonic acid (TfOH)[9] with respect to the donor. The donor was used in excess (1.1–1.5 equiv). The desired α-galactoside was not obtained with complete regioselectivity, although the yield was satisfactory in all the cases (entries 1–5). The best result was obtained under conditions in which the concentration had been diluted to 1.5 equiv with respect to the donor (entry 5). In this reaction, selective glycosylation of acceptor **6** with phenyl 1-thioglycoside derivative **7** gave the expected tetrasaccharide **8** (76.6%) and by-product **9** (15.7%); acetylation of **8** and **9** gave compounds **11** and **12**, respectively (Scheme 2). The ^{1}H NMR spectrum of **11** showed 9H signals at δ 5.97–5.59 (H-2, 3, 4 of Gal a, b, c) along with a signal at δ 4.87 (d, 1H, $J_{1,2} =$ 3.7 Hz, H-1d), indicating that the newly formed glycosidic linkage was α-type. Similarly, the ^{1}H NMR spectrum of **12** showed 8H signals at δ 6.10–5.66 (H-2,3,4 of Gal a,b and H-2,3 of Gal c) along with a signal at δ 4.93 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1d), indicating that the newly formed glycosidic linkage was α-type. In addition, compounds **11** and **12** could be distinguished by the presence of either a doublet peak at 5.97 ppm assigned to H-4 of Gal c of **11**, or one at 4.57 ppm assigned to H-4 of Gal c of **12**. Removal of the DTBS and benzyl groups from **11** by TBAF, catalytic hydrogenolysis over 10% Pd–C, and subsequent acetylation gave **13**. Selective removal of the 2-(trimethylsilyl)ethyl (SE) group with TFA in dichloromethane and treatment[10] with trichloroacetonitrile in the presence of DBU gave the corresponding α-trichloroacetimidate **14**. Glycosylation of (2*S*,3*R*)-3-*O*-benzoyl-2-hexadecanamido-4-octadecane-1,3-diol **15**[2] with glycosyl donor **14** was carried out in the presence of TMSOTf and 4 Å MS to afford the tetrasaccharide derivative **16** (52.2%). Finally, removal of the acyl groups of **16** under Zemplén conditions and column chromatography using a Sephadex LH-20 furnished the target glycolipid **2** (Scheme 3). The structure and purity of **2** were demonstrated by ^{1}H NMR and HR-FABMS data.

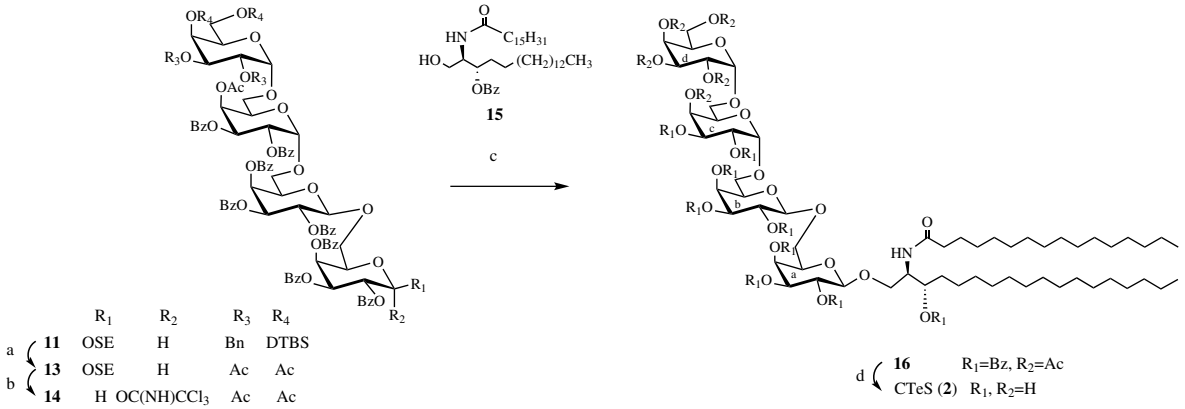
Next, the tetrasaccharide derivative **11** was converted into 4,6-diol acceptor **18** via debenzylation and benzoylation, followed by removal of the DTBS group. Glycosylation of **18** with **7** in the presence of NIS/TfOH gave the desired pentasaccharide **19**, along with a by-product **20** (mixed yield: 74.2%). As these compounds could not be separated at this stage. Therefore, their structures were confirmed after removal of the DTBS

Table 1. Galactosylation under various conditions

Entry	Donor **7**	Acceptor **6** (70 μmol)	Time	Promoter (equiv)	Solvent	Temp. (°C)	Product: yield (%)
1	1.1 equiv	1.0 equiv	30 min	NIS(1.0)–TfOH(0.05)	CH_2Cl_2 (1 mL)	−20	**8**: 59 **9**: 19
2	1.1 equiv	1.0 equiv	10 min	NIS(1.5)–TfOH(0.20)	CH_2Cl_2 (1 mL)	−20	**8**: 56 **9**: 12 **10**: 4
3	1.1 equiv	1.0 equiv	1 h	NIS(1.5)–TfOH(0.30)	CH_2Cl_2 (3 mL)	−60	**8**: 53 **9**: 16
4	1.5 equiv	1.0 equiv	30 min	NIS(1.5)–TfOH(0.30)	CH_2Cl_2 (1 mL)	−60	**8**: 51 **9**: 17 **10**: 14
5	1.5 equiv	1.0 equiv	30 min	NIS(1.5)–TfOH(0.30)	CH_2Cl_2 (3 mL)	−60	**8**: 77 **9**: 16



Scheme 2. Reagents and conditions: (a) NIS/TfOH, CH_2Cl_2, MS4 Å; (b) Ac_2O, Pyr.



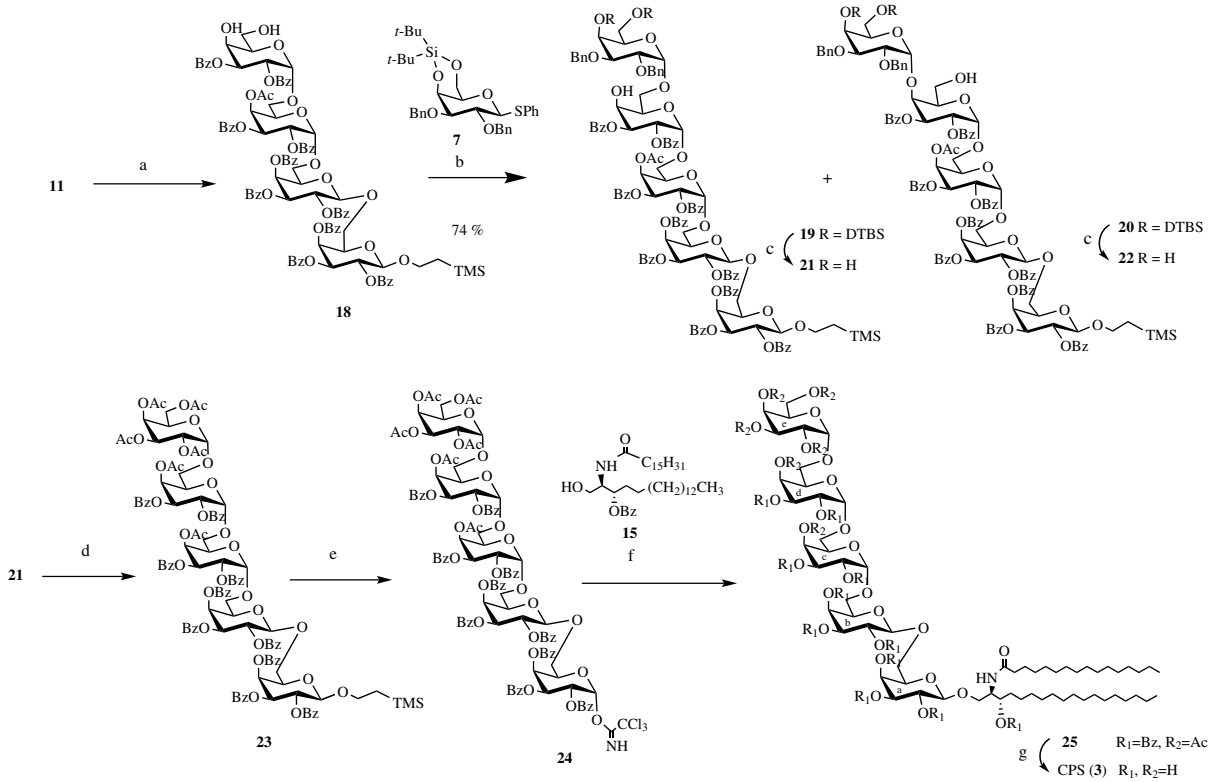
Scheme 3. Reagents and conditions: (a) (i) TBAF, AcOH/THF, 99%, (ii) Pd–C, H_2, MeOH/THF, (iii) Ac_2O, Pyr, 93% (two steps); (b) (i) TFA, CH_2Cl_2, (ii) CCl_3CN, DBU, CH_2Cl_2, 94% (two steps); (c) TMSOTf, MS4 Å, CH_2Cl_2, 52%; (d) NaOMe, 1,4-dioxane/MeOH, 88%.

group (**21:22** = 1.5:1). After removal of the DTBS group, debenzylation and acetylation of **19** gave **23**. Furthermore, **23** was distinguishable from the debenzylated and acetylated compound **22** based on the difference in chemical shifts of their ^{1}H NMR H-4 signals. The 2-(trimethylsilyl)ethyl group was removed with trifluoroacetic acid in dichloromethane and the 1-hydroxy compound was converted to imidate **24**. Glycosylation of **15** with glycosyl donor **24** was carried out in the presence of TMSOTf, giving the desired pentasaccharide derivative **25** (52.0%). Finally, removal of the acyl groups of **25** furnished the target glycolipid **3** (Scheme 4). The structure and purity of **3** were demonstrated by ^{1}H NMR and HR-FABMS data. In conclusion, a highly efficient and systematic synthesis of novel neutral glycosphingolipids from the *Zygomycetes* species *Mucor hiemalis* has been achieved.

1. Experimental

1.1. General

Optical rotations were measured with a Jasco P-1020 digital polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded with a JMN A500 FT NMR spectrometer with Me_4Si as the internal standard for solutions in $CDCl_3$. MALDI-TOFMS was recorded on a Perseptive Voyager RP mass spectrometer. High-resolution mass spectra were recorded on a JEOL JMS-700 under FAB conditions. TLC was performed on Silica Gel 60 F254 (E. Merck) with detection by quenching of UV fluorescence and by charring with 10% H_2SO_4. Column chromatography was carried out on Silica Gel 60 (E. Merck). Phenyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-β-D-galactopyranoside (**7**) and 2-(trimethylsilyl)ethyl



Scheme 4. Reagents and conditions: (a) (i) Pd–C, H_2, MeOH/THF, (ii) BzCl, Pyr, (iii) TBAF, AcOH/THF, 81%, (three steps); (b) NIS/TfOH, MS4 Å,CH_2Cl_2, **19**, **20** mix.,74%; (C) TBAF, AcOH/THF, **21**: 54%, **22**: 36%; (d) (i) Pd–C, H_2, MeOH/THF, (ii) Ac_2O, Pyr, 96%, (two steps); (e) (i) TFA, CH_2Cl_2, (ii) CCl_3CN, DBU, CH_2Cl_2, 91% (two steps); (f) TMSOTf, MS4 Å, CH_2Cl_2, 52%; (g) NaOMe, 1,4-dioxane/MeOH, 92%.

2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (**4**) were prepared as reported in our previous paper.[7]

1.2. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (5)

A solution of **4** (530 mg, 0.34 mmol) in THF (1.0 mL) and MeOH (2.0 mL) was stirred in the presence of 10% Pd–C (550 mg) for 1 h at room temperature under an H_2 atmosphere, then filtered and concentrated. The residue was benzoylated with benzoyl chloride (151 μL, 1.37 mmol) in pyridine (3 mL). The reaction mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed sequentially with 5% HCl, aq $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 20:1 toluene/acetone as the eluent to give **5** (496 mg, 85.5%): $[\alpha]_D^{24}$ +160.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16–7.24 (m, 40H, 8Ph), 5.97 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal b), 5.89 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal a), 5.86–5.77 (m, 3H, H-2 of Gal a, b, c), 5.61–5.56 (m, 3H, H-3 of Gal a, b, c), 5.21 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 5.00 (d, 1H, $J_{3,4} = 3.1$ Hz, H-4 of Gal c), 4.90 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.78 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 4.44 (d, 1H, $J_{6a,6b} = 12.2$ Hz, H-6a of Gal c), 4.33 (d, 1H, H-6b of Gal c), 4.23–4.17 (m, 3H, H-5 of Gal a, b, H-6a of Gal b), 4.05 (s, 1H, H-5 of Gal c), 4.00–3.90 (m, 2H, H-6b of Gal b, CH_2CH_2O), 3.73 (dd, 1H, $J_{5,6a} = 6.1$ Hz, $J_{6a,6b} = 11.0$ Hz, H-6a of Gal a), 3.58–3.52 (m, 2H, H-6b of Gal a, CH_2CH_2O), 1.20 and 1.04 (2s, 18H, 2 *t*-Bu), 0.94–0.76 (m, 2H, CH_2CH_2O), −0.15 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 165.9, 165.4, 165.2, 133.4, 133.1, 130.0, 129.8, 129.7, 129.5, 129.4, 129.0, 128.9, 128.5, 128.4, 128.3, 128.25, 128.20, 101.0 (C-1 of Gal b), 100.9 (C-1 of Gal a), 97.7 (C-1 of Gal c), 72.9, 72.1, 72.0, 71.8, 71.1, 70.9, 69.9, 69.8, 68.6, 68.3, 67.9, 67.54, 67.46, 67.4, 66.9, 66.6, 27.7, 27.5, 27.3, 23.2, 20.7, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{87}H_{92}O_{24}Si_2Na$ $[M+Na]^+$: *m*/*z* 1599.5. Found: *m*/*z* 1599.9.

1.3. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (6)

A solution of **5** (371 mg, 0.24 mmol) and acetic acid (61 μL, 1.1 mmol) in THF (2 mL) was treated with

1 M TBAF in THF (590 μL, 0.56 mmol) at room temperature and then was stirred for 12 h. After concentration, the residue was added to the water, extracted with ethyl acetate, and the organic layer was proceeded as usual. The product was purified by silica gel column chromatography using 3:1 toluene/acetone as the eluent to give **6** (322 mg, 95.3%): $[\alpha]_D^{24}$ +152.9 (*c* 0.8, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.13–7.26 (m, 40H, 8 Ph), 6.00 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal a), 5.93 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal b), 5.81–5.67 (m, 4H, H-2 of Gal a, b, c, H-3 of Gal c), 5.59–5.50 (m, 2H, H-3 of Gal a, b), 5.27 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 4.91 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.79 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 4.79 (s, 1H, H-4 of Gal c), 4.28–4.19 (m, 4H, H-5 of Gal a, b, H-6a of Gal c, H-6b of Gal c), 4.02 (d, 1H, $J_{5,6a} = 4.9$ Hz, H-5 of Gal c), 3.98–3.93 (m, 3H, H-6a of Gal a, H-6b of Gal a, CH_2CH_2O), 3.74–3.67 (m, 2H, H-6a of Gal b, H-6b of Gal b), 3.57 (dt, 1H, CH_2CH_2O), 0.95–0.74 (m, 2H, CH_2CH_2O), −0.17 (s, 9H, $Si(CH_3)_3$).^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 165.6, 165.5, 165.4, 165.2, 133.4, 133.2, 133.0, 130.0, 129.8, 129.74, 129.71, 129.5, 129.4, 129.2, 129.0, 128.9, 128.8, 128.54, 128.48, 128.34, 128.29, 128.2, 101.1 (C-1 of Gal b), 100.8 (C-1 of Gal a), 97.9 (C-1 of Gal c), 73.1, 72.3, 72.1, 72.0, 70.9, 70.3, 69.9, 69.7, 69.2, 68.8, 68.7, 68.1, 68.0, 67.6, 67.4, 62.7, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{79}H_{76}O_{24}SiNa$ $[M+Na]^+$: *m*/*z* 1459.4. Found: *m*/*z* 1459.5.

1.4. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→6)-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (8), 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (9)

A solution of compound **7** (61.8 mg, 0.10 mmol) and **6** (100 mg, 69.6 μmol) containing activated 4 Å MS (300 mg) in a dry CH_2Cl_2 (3 mL) was stirred under an atmosphere of argon for 2 h at room temperature. After cooling to −60 °C, successively NIS (35 mg, 0.85 mmol) and TfOH (2.8 μL, 0.17 mmol) were added and stirring was continued at −60 °C for 30 min, then neutralized with Et_3N. The reaction mixture was filtered, and the filtrate was washed with aq sodium thiosulfate, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 15:1 hexane/EtOAc as the eluent to give **8** (102 mg, 76.6%) and **9** (21.0 mg, 15.7%). Compound **8**: $[\alpha]_D^{24}$ +131.9 (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 5.13 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 4.91 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.79 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.68 (d, 1H, $J_{1,2} = 9.8$ Hz, H-1 of Gal a). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 165.8, 165.5, 165.4, 165.3, 165.2, 165.11, 165.08, 138.9, 138.1, 133.4, 133.3, 133.1, 133.03, 133.00, 132.8, 130.04, 129.96, 129.84, 129.78, 129.7, 129.6, 129.4, 129.2, 129.0, 128.8, 128.6, 128.5, 128.4, 128.3, 128.20, 128.15, 128.1, 127.7, 127.6, 127.4, 101.0 (C-1 of Gal b), 100.8 (C-1 of Gal a), 99.2 (C-1 of Gal d), 97.4 (C-1 of Gal c), 77.7, 73.9, 72.8, 72.2, 71.9, 71.7, 71.0, 70.9, 69.9, 69.8, 68.9, 68.8, 68.7, 68.5, 68.1, 67.7, 67.44, 67.38, 67.2, 66.5, 29.6, 27.6, 27.3, 23.4, 20.6, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{107}H_{114}O_{29}Si_2Na$ $[M+Na]^+$: *m*/*z* 1941.7. Found: *m*/*z* 1941.8. Compound **9**: $[\alpha]_D^{24}$ +122.2 (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 4.92 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 4.83 (d, 1H, $J_{1,2} = 7.97$ Hz, H-1 of Gal b), 4.71 (d, 1H, $J_{1,2} = 2.4$ Hz, H-1 of Gal d), 4.70 (d, 1H, $J_{1,2} = 9.8$ Hz, H-1 of Gal a). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 165.7, 165.4, 165.2, 138.7, 137.2, 133.3, 133.1, 132.9, 130.0, 129.74, 129.68, 129.4, 129.3, 129.2, 129.0, 128.8, 128.5, 128.4, 128.3, 128.2, 128.11, 128.05, 127.6, 101.0 (C-1 of Gal b), 100.7 (C-1 of Gal a), 100.4 (C-1 of Gal d), 97.4 (C-1 of Gal c), 77.5, 76.9, 74.73, 74.68, 73.0, 72.3, 72.0, 71.8, 70.8, 70.5, 70.02, 69.99, 69.8, 68.8, 68.6, 68.1, 67.8, 67.3, 67.1, 66.2, 60.1, 29.7, 27.6, 27.3, 23.4, 20.6, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{107}H_{114}O_{29}Si_2Na$ $[M+Na]^+$: *m*/*z* 1941.7. Found: *m*/*z* 1941.8.

1.5. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (11)

A solution of **8** (622 mg, 0.32 mmol) in pyridine (3 mL) and Ac_2O (2 mL) was stirred for 12 h at room temperature. Toluene was added and evaporated, then extracted with $CHCl_3$, washed with 5% HCl, aq $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 15:1 toluene/EtOAc as the eluent to give **11** (607 mg, 95.6%): $[\alpha]_D^{24}$ +126.9 (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.12–7.26 (m, 50H, 10Ph), 5.97 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal c), 5.90 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal b), 5.87–5.78 (m, 4H, H-2 of Gal a, 2 of Gal b, 3 of Gal c, 4 of Gal a), 5.69 (dd, 1H, $J_{1,2} = 3.7$ Hz, $J_{2,3} = 10.4$ Hz, H-2 of Gal c), 5.63 (dd, 1H, $J_{2,3} = 10.4$ Hz, H-3 of Gal b), 5.59 (dd, 1H, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 3.1$ Hz, H-3 of Gal a), 5.21 (d, 1H, H-1 of Gal c), 4.95–4.81 (m, 4H, 2 benzylmethylene), 4.91 (d, 1H, $J_{1,2} = 8.6$ Hz, H-1 of Gal b), 4.87 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.74 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 4.59 (d, 1H, $J_{3,4} = 3.1$ Hz, H-4 of Gal d), 4.43 (t, 1H,

$J_{5,6a} = J_{5,6b} = 6.1$ Hz, H-5 of Gal a), 4.32–4.24 (m, 3H, H-6a of Gal b, c, H-6b of Gal c), 4.21–4.17 (m, 2H, H-6a of Gal d, H-6b of Gal d), 4.11 (dd, 1H, $J_{2,3} = 10.4$ Hz, H-2 of Gal d), 4.02–3.97 (dd, 1H, CH_2CH_2O), 3.93 (dd, 1H, H-3 of Gal d), 3.88 (dd, 1H, $J_{5,6b} = 6.7$ Hz, $J_{6a,6b} = 9.8$ Hz, H-6b of Gal b), 3.83–3.76 (m, 4H, H-5 of Gal b, c, d, H-6a of Gal a), 3.59–3.52 (m, 2H, H-6b of Gal a, CH_2CH_2O), 2.18 (s, 3H, Ac), 1.16 and 1.12 (2s, 18H, 2 *t*-Bu), 0.94–0.76 (m, 2H, CH_2CH_2O), −0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 166.1, 165.4, 165.2, 165.1, 139.1, 138.6, 137.8, 133.3, 132.0, 130.0, 129.8, 129.74, 129.68, 129.6, 129.5, 129.4, 129.3, 129.0, 128.8, 128.5, 128.43, 128.38, 128.3, 128.2, 128.2, 128.11, 128.08, 127.7, 127.6, 127.34, 127.25, 100.9 (C-1 of Gal b), 100.8 (C-1 of Gal a), 99.0 (C-1 of Gal d), 97.2 (C-1 of Gal c), 77.6, 74.4, 73.6, 72.7, 72.0, 71.9, 71.8, 71.14, 71.06, 70.0, 69.8, 68.7, 68.5, 68.2, 68.0, 67.7, 67.3, 67.1, 66.9, 66.3, 27.7, 27.3, 23.3, 21.4, 20.62, 20.59, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{109}H_{116}O_{30}Si_2Na$ $[M+Na]^+$: *m*/*z* 1983.7. Found: *m*/*z* 1983.4.

1.6. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-6-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (12)

Compound **12** was derived according to the procedure described for the treatment of **11**. Compound **9** (275 mg, 0.14 mmol)→**12** (255 mg, 90.7%): $[\alpha]_D^{24}$ +139.9 (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.18–7.22 (m, 50H, 10 Ph), 6.10 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal b), 5.97 (d, 1H, $J_{3,4} = 3.7$ Hz, H-4 of Gal a), 5.90–5.84 (m, 2H, H-2 of Gal a, 2 of Gal b), 5.79–5.66 (m, 4H, H-2 of Gal c, H-3 of Gal a, b, c), 5.17 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal c), 4.99 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.98–4.79 (m, 4H, 2 benzylmethylene), 4.93 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal d), 4.87 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 4.66 (s, 1H, H-4 of Gal d), 4.57 (br d, H-4 of Gal c), 2.21 (s, 3H, Ac), 1.13 and 1.06 (2s, 18H, 2 *t*-Bu), 0.91–0.72 (m, 2H, CH_2CH_2O), −0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 165.7, 165.6, 165.2, 189.0, 138.2, 133.3, 133.0, 130.1, 130.0, 129.82, 129.76, 129.7, 129.4, 129.2, 129.0, 128.8, 128.6, 128.5, 128.4, 128.34, 128.26, 128.2, 128.1, 127.6, 127.5, 127.3, 100.9 (C-1 of Gal b), 100.7 (C-1 of Gal a), 100.4 (C-1 of Gal d), 96.8 (C-1 of Gal c), 77.8, 76.4, 74.0, 73.8, 73.2, 72.4, 71.9, 71.7, 70.8, 70.6, 70.3, 70.1, 69.9, 69.7, 69.0, 68.4, 68.2, 68.1, 67.3, 66.9, 66.1, 62.9, 27.6, 27.2, 23.3, 20.9, 20.7, 17.6 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{109}H_{116}O_{30}Si_2Na$ $[M+Na]^+$: *m*/*z* 1983.7. Found: *m*/*z* 1983.5.

1.7. 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (13)

A solution of **11** (400 mg, 0.20 mmol) and acetic acid (53 μL, 0.31 mmol) in THF (2 mL) was treated with 1 M TBAF in THF (408 μL, 0.41 mmol) at room temperature and then was stirred for 12 h. After concentration, the residue was added to the water, extracted with ethyl acetate, and the organic layer was proceeded as usual. The product was purified by silica gel column chromatography using 5:1 toluene/acetone as the eluent to give the diol compound (366 mg, 98.5%). To a solution of the compound (366 mg, 0.29 mmol) in THF (1.5 mL) and MeOH (3.0 mL) was stirred in the presence of 10% Pd–C (400 mg) for 1 h at room temperature under an H_2 atmosphere, then filtered and concentrated. The residue was treated with Ac_2O (2 mL) in pyridine (3 mL). The reaction mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed sequentially with 5% HCl, aq $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 10:1 toluene/acetone as the eluent to give **13** (356 mg, 93.0%). $[\alpha]_D^{24}$ +125.3 (*c* 1.2, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.12–7.26 (m, 40H, 8Ph), 5.19 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal c), 5.04 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal d), 4.97 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.82 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 2.25, 2.21, 2.20, 2.11 and 2.10 (each s, 15H, 5Ac), 0.94–0.77 (m, 2H, CH_2CH_2O), −0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.4, 170.2, 169.9, 169.6, 166.1, 165.4, 165.3, 165.2, 165.1, 133.33, 133.26, 133.1, 133.0, 130.1, 130.0, 129.8, 129.73, 129.68, 129.5, 129.4, 129.2, 129.0, 128.9, 128.5, 128.29, 128.26, 128.2, 128.13, 101.0 (C-1 of Gal b), 100.8 (C-1 of Gal a), 97.5 (C-1 of Gal c), 96.9 (C-1 of Gal d), 72.7, 71.9, 71.8, 70.0, 69.9, 68.6, 68.5, 68.1, 67.9, 67.5, 67.4, 67.3, 66.5, 66.1, 65.7, 61.7, 20.6, 20.5, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{95}H_{96}O_{34}SiNa$ $[M+Na]^+$: *m*/*z* 1831.5. Found: *m*/*z* 1831.7.

1.8. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate (14)

To a solution of **13** (283 mg, 0.16 mmol) in CH_2Cl_2 (2.0 mL), cooled to 0 °C, was added trifluoroacetic acid (4.0 mL) and the mixture was stirred for 1.5 h at room temperature and concentrated. Ethyl acetate and toluene (1:2) were added and evaporated to give the

1-hydroxy compound. To a solution of the residue in CH_2Cl_2 (2.0 mL) cooled at 0 °C were added trichloroacetonitrile (157 μL, 1.56 mmol) and DBU (23 μL, 0.16 mmol). The reaction mixture was stirred for 1.5 h at 0 °C. After completion of the reaction, the mixture was concentrated. Column chromatography of the residue on silica gel (1:2 hexane/ethyl acetate) gave **14** (272 mg, 94.0%): $[\alpha]_D^{24}$ +145.7 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51–7.17 (m, 41H, 8Ph, NH), 6.76 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal a), 5.06 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 4.93 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal d), 4.83 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 2.13, 2.090, 2.086, 1.99 and 1.97 (each s, 15H, 5Ac). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.3, 170.1, 169.8, 169.6, 166.1, 165.6, 165.3, 165.1, 160.4, 133.4, 133.2, 133.1, 133.0, 130.0, 129.9, 129.8, 129.7, 129.5, 129.3, 129.0, 128.8, 128.6, 128.4, 128.3, 128.2, 128.1, 101.0 (C-1 of Gal b), 97.4 (C-1 of Gal c), 96.9 (C-1 of Gal d), 93.6 (C-1 of Gal a), 90.7 (CCl_3), 71.8, 71.0, 69.7, 68.8, 68.5, 68.3, 68.2, 68.1, 67.9, 67.6, 67.41, 67.38, 66.5, 66.2, 65.7, 61.70, 61.65, 20.6, 20.5. MALDI-TOFMS: calcd for $C_{92}H_{84}Cl_3NO_{34}Na$ $[M+Na]^+$: *m*/*z* 1874.4. Found: *m*/*z* 1875.8.

1.9. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→1)-(2*S*,3*R*)-3-*O*-benzoyl-2-hexadecanamidooctadecane-1,3-diol (16)

To a solution of **14** (68 mg, 36.7 μmol) and (2*S*,3*R*)-3-*O*-benzoyl-2-hexadecanamido-4-octadecane-1,3-diol **15** (47 mg, 73.4 μmol) in dry CH_2Cl_2 (1.0 mL) was added 4 Å MS (500 mg), and the mixture was stirred for 2 h at room temperature, then cooled to 0 °C. TMSOTf (6 μL, 33.0 μmol) was added, and the mixture was stirred for 1.5 h at 0 °C, then neutralized with Et_3N. The solids were filtrated off and washed with $CHCl_3$. The combined filtrate and washings were successively washed with water, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 3:1 toluene/EtOAc as the eluent to give **16** (44.7 mg, 52.2%). $[\alpha]_D^{24}$ +96.8 (*c* 0.4, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11–7.19 (m, 45H, 9Ph), 5.17 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 4.92 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.56 (d, 1H, $J_{1,2} = 7.3$Hz, H-1 of Gal b), 4.36 (d, 1H, $J_{1,2} = 7.9$Hz, H-1 of Gal a), 2.12, 2.09, 2.07, 1.98 and 1.95 (each s, 15H, 5Ac), 1.75–1.09 (m, 54H, 27 $-CH_2-$), 0.88 (t, 6H, $2CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 170.7, 170.3, 170.1, 169.8, 169.6, 166.1, 165.4, 165.3, 165.2, 165.1, 165.0, 133.5, 133.4, 133.3, 133.1, 133.0, 132.8, 130.7, 130.2, 130.0, 129.9, 129.8, 129.73, 129.66, 129.6, 129.5, 129.4, 129.3, 129.0, 128.8, 128.6, 128.5, 128.4, 128.31, 128.26, 128.18, 128.15, 125.8, 101.1 (C-1 of Gal b), 100.5 (C-1 of Gal a), 97.6 (C-1 of Gal c), 97.0 (C-1 of Gal d), 73.4, 72.8, 71.8, 71.7, 71.44, 71.36, 70.6, 69.8, 68.5, 68.4, 68.3, 68.1, 67.9, 67.8, 67.6, 67.43, 67.39, 66.9, 66.5, 66.1, 65.8, 61.7, 50.1, 36.9, 36.5, 31.9, 31.5, 29.7, 29.6, 29.5, 29.3, 29.1, 25.7, 25.6, 25.5, 22.7, 20.6, 20.5, 14.1. MALDI-TOFMS: calcd for $C_{131}H_{155}NO_{37}Na$ $[M+Na]^+$: *m*/*z* 2357.0. Found: *m*/*z* 2357.1.

1.10. α-D-Galactopyranosyl-(1→6)-α-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosiyl-(1→1)-(2*S*,3*R*)-2-hexadecanamido-octadecane-1,3-diol (2)

To a solution of **16** (28.5 mg, 12.2 μmol) in MeOH (1.0 mL) and 1,4-dioxane (1.0 mL) was added NaOMe (25 mg) at room temperature and the mixture was stirred for 12 h, then neutralized with Amberlite IR 120[H^+]. The mixture was filtered off and concentrated. The product was purified by sephadex LH-20 column chromatography (1:1 $CHCl_3$/MeOH) to give **2** (12.7 mg, 87.6%): $[\alpha]_D^{24}$ +54.4 (*c* 0.3, $CHCl_3$/MeOH = 1:1). ^{1}H NMR (500 MHz, DMSO-d_6–D_2O) δ 4.72 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 4.69 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal d), 4.17 (d, 1H, $J_{1,2} = 7.3$ Hz, H-1 of Gal b), 4.07 (br d, 1H, H-1 of Gal a), 1.58–1.08 (m, 54H, 27 $-CH_2-$), 0.82 (t, 6H, 2 CH_3). HR-FABMS: calcd for $C_{58}H_{109}NO_{23}Na$ $[M+Na]^+$: *m*/*z* 1210.7288. Found: *m*/*z* 1210.7238.

1.11. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (18)

To a solution of **11** (220 mg, 0.11 mmol) in THF (1.5 mL) and MeOH (3.0 mL) was added 10% Pd–C (250 mg), and the reaction mixture was stirred in a H_2 atmosphere for 40 min. at room temperature, then filtered and concentrated. The residue was benzoylated with benzoyl chloride (52 μL, 0.45 mmol) in pyridine (3 mL) for 3 h. The reaction mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed sequentially with 5% HCl, aq $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 10:1 toluene/acetone as the eluent to give the compound (212 mg, 94.8%). A solution of this compound (221 mg, 0.22 mmol) and acetic acid(29 μL, 0.50 mmol)in THF (2 mL) was treated with 1M TBAF in THF (222 μL, 0.22 mmol) at room temperature and then was stirred for 12 h. After concentration, the residue was added to the water, extracted with ethyl acetate, and the organic

layer was proceeded as usual. The product was purified by silica gel column chromatography using 5:1 toluene/acetone as the eluent to give **18** (177 mg, 85.8%): $[\alpha]_D^{24}$ +138.1 (*c* 2.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.19–7.28 (m, 50H, 10Ph), 5.47 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 5.22 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 5.05 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.86 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 2.16 (s, 3H, Ac), 0.97–0.81 (m, 2H, CH_2CH_2O), −0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 166.1, 166.0, 165.7, 165.6, 165.44, 165.41, 165.2, 165.13, 165.10, 133.3, 133.0, 130.0, 129.9, 129.8, 129.69, 129.66, 129.5, 129.31, 129.27, 129.1, 129.0, 128.8, 128.7, 128.43, 128.36, 128.3, 128.21, 128.18, 128.15, 128.1, 101.0 (C-1 of Gal b), 100.7 (C-1 of Gal a), 98.0 (C-1 of Gal c), 97.6 (C-1 of Gal d), 72.8, 72.0, 71.8, 71.0, 70.2, 69.9, 69.8, 69.2, 68.8, 68.6, 68.5, 68.0, 67.8, 67.54, 67.51, 67.3, 66.7, 62.6, 20.4, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{101}H_{96}O_{32}SiNa$ $[M+Na]^+$: *m*/*z* 1871.6. Found: *m*/*z* 1871.3.

1.12. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→6)-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (19), 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (20)

Compound **20** was derived according to the procedure described for the treatment of **8**. Compound **18** (146 mg, 78.7 μmol)→**20** (136 mg, 74.2%): MALDI-TOFMS: calcd for $C_{129}H_{134}O_{37}Si_2Na$ $[M+Na]^+$: *m*/*z* 2353.8. Found: *m*/*z* 2353.2.

1.13. 2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→6)-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (21), 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (22)

Compounds **21** and **22** were derived according to the procedure described for the treatment of **6**. Compounds **19** and **20** (136 mg, 58.4 μmol)→**21** (69.3 mg, 54.1%) and **22** (46.1 mg, 36.0%): $[\alpha]_D^{24}$ +135.1 (*c* 0.9, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.00–7.15 (m, 60H, 12Ph), 5.32 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 5.13 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal e), 5.00 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.87 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.69 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal a), 2.06 (s, 3H, Ac), 0.83–0.66 (m, 2H, CH_2CH_2O), −0.13 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 166.1, 166.0, 165.8, 165.5, 165.31, 165.26, 165.2, 165.1, 138.1, 133.3, 133.2, 133.0, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.2, 129.0, 128.9, 128.8, 128.44, 128.39, 128.3, 128.23, 128.15, 127.7, 100.9 (C-1 of Gal b), 100.7 (C-1 of Gal a), 98.4 (C-1 of Gal e), 97.6 (C-1 of Gal c), 97.3 (C-1 of Gal d), 77.5, 75.3, 73.4, 72.7, 72.6, 72.0, 71.8, 71.7, 71.0, 70.02, 69.98, 69.8, 68.9, 68.8, 68.5, 68.3, 67.9, 67.6, 67.34, 67.28, 67.2, 66.9, 66.4, 62.8, 29.6, 20.5, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{121}H_{118}O_{37}SiNa$ $[M+Na]^+$: *m*/*z* 2213.7. Found: *m*/*z* 2213.3. Compound **22**: $[\alpha]_D^{24}$ +132.5 (*c* 0.6, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.00–7.16 (m, 60H, 12 Ph), 5.06 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 5.04 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.82 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal e), 4.67 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.66 (d, 1H, $J_{1,2} = 8.5$Hz, H-1 of Gal a), 4.47 (br d, 1H, H-4 of Gal d), 2.04 (s, 3H, Ac), 0.89–0.67 (m, 2H, CH_2CH_2O), −0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 166.1, 166.0, 165.4, 165.3, 165.18, 165.15, 165.1, 137.7, 137.1, 133.3, 133.2, 133.1, 133.0, 130.1, 130.04, 129.96, 129.9, 129.8, 129.7, 129.6, 129.4, 129.33, 129.28, 129.2, 129.1, 128.6, 128.53, 128.46, 128.4, 128.3, 128.2, 128.13, 128.10, 128.0, 127.9, 127.8, 100.8 (C-1 of Gal a, b), 100.3 (C-1 of Gal e), 97.9 (C-1 of Gal c), 97.4 (C-1 of Gal d), 77.6, 77.5, 76.3, 74.8, 72.7, 72.3, 72.02, 71.97, 71.8, 70.8, 70.7, 70.0, 69.9, 68.6, 68.51, 68.45, 68.3, 68.1, 67.8, 67.4, 67.0, 66.5, 66.4, 62.9, 60.5, 27.2, 20.5, 17.7 (–OCH_2CH_2), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{121}H_{118}O_{37}SiNa$ $[M+Na]^+$: *m*/*z* 2213.7. Found: *m*/*z* 2213.6.

1.14. 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (23)

To a solution of **21** (69.3 mg, 31.6 μmol) in THF (0.4 mL) and MeOH (0.8 mL) was added 10% Pd–C (80 mg), and the reaction mixture was stirred in a H_2 atmosphere for 3 h at room temperature, then filtered and concentrated. The residue was acetylated with Ac_2O (1 mL) in pyridine (1.5 mL). The reaction mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed sequentially with 5% HCl, aq

$NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography using 10:1 toluene/acetone as the eluent to give **23** (67.5 mg, 96.1%). $[\alpha]_D^{24}$ +172.3 (*c* 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.00–7.17 (m, 50H, 10Ph), 5.86–5.16 (m, 15H, H-2 of Gal a, b, c, d, e, H-3 of Gal a, b, c, d, e, H-4 of Gal a, b, c, d, e), 5.21 (d, 1H, $J_{1,2} = 3.6$ Hz, H-1 of Gal c), 5.07 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal e), 4.99 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal d), 4.81 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 4.67 (d, 1H, $J_{1,2} = 7.9$Hz, H-1 of Gal a), 2.35, 2.134, 2.128, 2.12, 2.05 and 2.04 (each s, 18H, 6Ac), 0.81–0.71 (m, 2H, CH_2CH_2O), −0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.4, 170.2, 169.9, 169.8, 166.2, 166.0, 165.4, 165.23, 165.16, 165.0, 153.4, 138.5, 133.2, 133.0, 130.1, 130.0, 129.8, 129.7, 129.5, 129.4, 129.3, 129.1, 129.0, 128.9, 128.5, 128.44, 128.38, 128.3, 128.2, 128.1, 125.3, 124.9, 100.8 (C-1 of Gal b), 100.7 (C-1 of Gal a), 97.40 (C-1 of Gal c), 97.37 (C-1 of Gal e), 96.5 (C-1 of Gal d), 72.7, 71.9, 71.8, 70.0, 69.9, 68.8, 68.7, 68.6, 68.4, 68.3, 68.1, 67.8, 67.7, 67.6, 67.5, 67.3, 67.0, 66.8, 66.6, 66.2, 61.9, 29.7, 21.4, 20.7, 20.6, 20.5, 17.7 ($-OCH_2CH_2$), −1.5 ($Si(CH_3)_3$). MALDI-TOFMS: calcd for $C_{117}H_{116}O_{42}SiNa$ $[M+Na]^+$: *m*/*z* 2243.7. Found: *m*/*z* 2243.9.

1.15. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-2,3,4-tri-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate (24)

Compound **24** was derived according to the procedure described for the treatment of **14**. Compound **23** (102 mg, 45.5 μmol)→**24** (95.2 mg, 91.3%): $[\alpha]_D^{24}$ +155.3 (*c* 0.8, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.65–7.16 (m, 50H, 11 Ph, NH), 6.77 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal a), 5.20 (d, 1H, $J_{1,2} = 3.1$Hz, H-1 of Gal c), 5.04 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal e), 4.99 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.78 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1 of Gal b), 2.16, 2.134, 2.128, 2.12, 2.05 and 1.97 (each s, 18H, 6Ac). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.6, 170.4, 170.2, 168.9, 169.8, 166.1, 166.0, 165.6, 165.3, 165.24, 165.21, 165.16, 165.03, 165.00, 160.5, 133.4, 133.2, 133.0, 130.1, 129.9, 129.7, 129.5, 129.4, 129.3, 129.0, 128.9, 128.8, 128.6, 128.5, 128.3, 128.2, 128.1, 100.7 (C-1 of Gal b), 97.4 (C-1 of Gal c), 97.3 (C-1 of Gal e), 96.5 (C-1 of Gal d), 93.7 (C-1 of Gal a), 90.7 (CCl_3), 71.8, 71.7, 70.8, 69.8, 68.8, 68.7, 69.6, 68.4, 68.3, 68.1, 67.8, 67.7, 67.6, 67.5, 67.0, 66.64, 66.59, 66.5, 66.2, 61.9, 29.7, 20.6. MALDI-TOFMS: calcd for $C_{114}H_{104}Cl_3NO_{42}Na$ $[M+Na]^+$: *m*/*z* 2286.5. Found: *m*/*z* 2287.4.

1.16. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-galacto-pyranosyl-(1→1)-(2*S*,3*R*)-3-*O*-benzoyl-2-hexadecanamidooctadecane-1,3-diol (25)

Compound **25** was derived according to the procedure described for the treatment of **16**. Compound **24** (50.0 mg, 22.1 μmol)→**25** (31.5 mg, 52.0%). $[\alpha]_D^{24}$ +117.2 (*c* 0.8, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.08–7.17 (m, 55H, 11 Ph), 5.20 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal c), 5.06 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1 of Gal e), 4.95 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1 of Gal d), 4.52 (d, 1H, $J_{1,2} = 7.3$ Hz, H-1 of Gal b), 4.36 (d, 1H, $J_{1,2} = 7.3$ Hz, H-1 of Gal a), 2.14, 2.12, 2.11, 2.04, 2.03 and 1.94 (each s, 18H, 6Ac), 1.75–1.07 (m, 54H, 27 $-CH_2-$), 0.88 (t, 6H, $2CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 170.7, 170.4, 170.2, 169.9, 169.7, 166.1, 165.9, 165.5, 165.3, 165.2, 165.0, 133.4, 133.3, 133.1, 133.0, 132.8, 131.0, 130.6, 130.1, 130.0, 129.74, 129.68, 129.6, 129.41, 129.36, 129.3, 129.2, 129.0, 128.9, 128.6, 128.5, 128.4, 128.34, 128.25, 128.2, 128.1, 101.0 (C-1 of Gal b), 100.7 (C-1 of Gal a), 97.6 (C-1 of Gal c), 97.4 (C-1 of Gal e), 96.6 (C-1 of Gal d), 75.7, 73.6, 72.9, 71.8, 71.4, 71.3, 70.6, 69.8, 68.8, 68.6, 68.49, 68.45, 68.4, 68.3, 68.1, 67.7, 67.6, 67.5, 67.1, 67.0, 66.6, 66.1, 61.9, 56.8, 50.2, 36.9, 36.5, 31.9, 31.5, 29.7, 29.6, 29.3, 29.1, 28.9, 27.9, 25.5, 25.2, 24.1, 22.7, 20.7, 20.6, 14.1, 1.0. MALDI-TOFMS: calcd for $C_{153}H_{175}NO_{45}Na$ $[M+Na]^+$: *m*/*z* 2769.1. Found: *m*/*z* 2769.1.

1.17. α-D-Galactopyranosyl-(1→6)-α-D-galactopyranosyl-(1→6)-α-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→6)-β-D-galactopyranosyl-(1→1)-(2*S*,3*R*)-2-hexadecanamidooctadecane-1,3-diol (3)

Compound **3** was derived according to the procedure described for the treatment of **2**. Compound **25** (23.0 mg, 8.37 μmol)→**2** (10.4 mg, 92.0%). $[\alpha]_D^{24}$ +20.9 (*c* 0.04, $CHCl_3$/MeOH = 1:1). ^1H NMR (500 MHz, DMSO-d_6/D_2O) δ 4.59 (br d, 3H, H-1 of Gal c, d, e), 4.17 (d, 1H, $J_{1,2} = 6.7$ Hz, H-1 of Gal b), 4.07 (d, 1H, $J_{1,2} = 7.3$ Hz, H-1 of Gal a), 1.60–1.10 (m, 54H, 27 $-CH_2-$), 0.83 (t, 6H, $2CH_3$). HR-FABMS: calcd for $C_{64}H_{119}NO_{28}Na$ $[M+Na]^+$: *m*/*z* 1372.7816. Found: *m*/*z* 1372.7858.

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